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PANEL DISCUSSION ON THE CLINICAL MANAGEMENT OF SKIN DISEASE IN GERIATRIC PATIENTS*

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MODERATOR NELSON: We intend to consider some of the common problems of importance with regard to aging skin.

I propose to ask each panelist to discuss briefly a number of questions that I shall present to him. Time will not permit us to cover the subject completely, and I am sure that questions will arise which you may wish to have answered. Therefore, we hope to be able to spend half an hour at the end of the discussion answering specific questions from the audience.

Perhaps nowhere in the body are changes caused by age more apparent than in the skin. The skin so mirrors the changes brought about by time and by exposure to the rigors of civilization, that its appearance becomes a yardstick used by physicians and laymen alike to estimate a person's age. The loss of elasticity in the skin results in wrinkles that become noticeable rather early on the face and neck, much to the chagrin of middle-aged people. As time goes on, these changes become more and more pronounced and extend more or less to the whole body.

Dr. Rothman, how does the skin in elderly persons differ from the skin in a young adult? What important anatomic and physiologic changes occur? What changes predispose toward skin problems in the aged? Are there any local or general measures that can be taken to delay or prevent these signs of age? Should we use hormone creams to try to prevent these changes?

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† Deceased, May 15, 1957.

DR. ROTHMAN: The surface of old skin appears wrinkled and is usually a bit more shiny than that of young skin. There is a tendency toward dryness and cracking of the surface layer.

The skin of elderly persons lacks elasticity. Coarse wrinkles appear over the edges of the mimic muscles. The loss of fat commonly observed leads to redundancy of the skin, which is no longer sufficiently elastic to take up the slack.

With regard to loss of elasticity, the normal skin is stretched to some degree on the underlying tissue like a tight glove that is forced on the hand. Cutaneous stretchability is much greater in the young than in the old. The skin in the elderly person, therefore, shows little resistance to slight stretching in the beginning because it has no initial tension. Upon harder stretching, however, there is increased resistance. The skin expands relatively less because of the intertwining of fibers resulting from the decrease in the ground substance between them.

One should distinguish true senile changes from changes on exposed parts due to sunshine, wind and weather. The older a person grows, the longer the exposure. We may find so-called senile changes in relatively young people, too, in the exposed parts—mainly "senile elastosis," representing degeneration of collagen fibers.

Then there is the question about the use of estrogenic creams. Flattening of the papillae in the upper corium is one of the most characteristic changes in senile skin, and existing data indicate that fibroblastic activity increases upon local application of estrogens to the thinned and senile skin of women. Reconstruction of the papillary bodies has been claimed, but experimentation has not been thorough enough to confirm it. However, one thing seems to be true—the water content of the tissue increases upon the local application of estrogens. I oppose the use of such materials simply because it has not been well established that there are no adverse effects from too much absorption of estrogen. The manufacturers of estrogen creams claim that the concentration is so low that no untoward systemic effects can occur.

Actually, an impatient elderly woman who wants to be rejuvenated overnight will apply so much estrogen cream and so frequently that we cannot gauge the total amount. Therefore, I am opposed to the sale of estrogen creams. It is true that harmful effects have not been reported. On the other hand, a gynecologist rarely asks a woman who has spot bleeding from the vagina whether or not she has used estrogenic creams.

MODERATOR NELSON: Dr. Rothman, are there other perhaps less harmful ways of keeping the skin youthful?

DR. ROTHMAN: I think it is all right to grow old. I believe that dryness of the skin can be counteracted by simple lubrication with so-called lubricating creams and cold creams which will improve the appearance of the surface. Lubrication will do nothing to the wrinkles already there.

MODERATOR NELSON: A certain amount of dryness and wrinkling, then, is inevitable?

DR. ROTHMAN: I believe so. However, you can mask it with cosmetics.

MODERATOR NELSON: Dr. Rothman points out the inevitability of changes that accompany age. These changes can often lead to itching; so much so that itching of the aging skin is given a special diagnostic category and called senile pruritus. It sometimes can be exceedingly severe. In fact, generalized itching without apparent skin lesions, except for excoriations, is probably the most frequent dermatologic complaint of old age.

I should like to know how Dr. Rein manages the elderly patient who comes into his office during the colder months of the year complaining of generalized pruritus but having little to show for the symptoms except a few excoriations. How do you approach the problem of the dry, aging skin? How do you hydrate the skin of a patient with senile pruritus? How do you control or attempt to elevate the threshhold of itching? Do you use sedation? What kind? Do you use antihistamines? Dr. Rein.

DR. REIN: The term senile pruritus is applied loosely to any form of itching that occurs in an elderly patient. To define dry skin is not simple, because the dryness may be a matter of degree or merely a sensation that the patient has. "Geriatric skin" is a bad term because the clinical age of the patient frequently does not agree with his chronologic age. For example, xerosis is probably the best term for acquired dryness, whereas asteatosis signifies a total absence of sebum as the result of sebaceous atrophy. Senile pruritus should, therefore, be classified as that form of itching due to atrophic and degenerative changes in the skin, especially over the trunk.

When xerosis (or acquired dryness) occurs in an elderly person with an asteatotic skin, it presents a difficult problem, because atrophy of the sweat and sebaceous glands and thinning of the skin make the condition much more susceptible to aggravation by soap and water, chemicals, irritants and changes in the weather.

Dr. Nelson's question dealt with the management of pruritus in the elderly patient with a dry skin, generalized itching, and nothing else but a number of excoriations. Treatment should be along the following lines: First, hydrate and soften the skin. The application of a preparation of the water-in-oil type will prove helpful in counteracting the demulsifying action of soap and water. Many preparations available commercially permit hydration of the deeper layers of the skin and often afford dramatic relief of pruritus.

Second is the application of animal, vegetable or mineral oil to the skin prior to bathing, to protect it from detergent action. Two preparations, which I have found satisfactory, are 10 per cent olive oil, 20 per cent water, and 70 per cent lanolin; or 1 per cent lecithin, 2 per cent cholesterol, and equal parts of lanolin and soybean oil. The last 2 ingredients are the important ones in overcoming the so-called dryness.

Third, shower baths should be discontinued. Colloidal baths are valuable. Such a bath is prepared as follows: a cup of starch, bran or oatmeal is shaken in a quart milk bottle with 2 teaspoonfuls of a lubricating oil and then thoroughly mixed with a quart of milk and poured into half a tubful of lukewarm water. These patients should be instructed to avoid the use of soap, or at least

to limit its use to the axillae, groins and feet. They should not rub themselves with a towel, but pat themselves dry. After the bath they should again grease and soften the skin with one of the oily preparations.

Fourth, it is sometimes possible to elevate the threshhold for the perception of itching by mild sedation. This is best accomplished by the oral administration of those antihistamines that have a definite sedative or hypnotic action. Phenergan and Benadryl often produce such effects.

The local application of antihistamine preparations must be discouraged because of the great danger of sensitization. Not long ago, a questionnaire was sent to dermatologists asking about their use of antihistaminic ointments. I am certain that most dermatologists discourage their use because 10 to 20 per cent of patients who use these ointments over a long period of time have severe reactions.

When the pruritus is severe enough to interfere with sleep, the administration of a tranquilizing drug may afford the patient much needed rest and diminish the uncontrollable desire to scratch, especially during the night. I want to emphasize that tranquilizing drugs do not cure anything. They are not used to cure a skin disease, but they are of value in calming the patient, affording him natural sleep, and sometimes preventing much so-called nocturnal itching.

MODERATOR NELSON: Thank you, Dr. Rein. The audience and the other panelists may wish to question you later about some of the points you have mentioned, but for the moment it strikes me that you have answered my questions very well. On the other hand, we know that pruritus may also be a symptom of serious systemic disease. How do you determine whether pruritus in an oldster is due primarily to local factors or whether it is a manifestation of an underlying disease?

DR. REIN: That is a difficult question to answer because time will not permit reviewing the various laboratory and clinical regimens that must be followed in order to exclude underlying diseases. When an elderly patient itches, it does not necessarily mean that the itching is due to dry skin. He may have an important systemic disease. It is embarrassing to treat a patient with lubricating oils and find that he is due to die from some underlying disease. A large number of these disorders must be kept in mind, *e.g.*, diabetes, nephritis, hepatitis, carcinoma, leukemia, Hodgkin's disease, tuberculosis, gout, thyroid dysfunction, climacteric changes, local infections, drug or food allergy, and even psychogenic factors. A physician, and a dermatologist particularly, must be aware of the various conditions other than simple dryness that may cause pruritus.

MODERATOR NELSON: Your summary is excellent, Dr. Rein.

I should like to turn now to some of the other members of the panel. Dr. Traub—associated with the process of aging are a number of cutaneous new growths that physicians in general often have great difficulty in identifying. Many of these are purely cosmetic problems, but in some cases these lesions are of considerable significance, in that they may be precancerous or may predispose to malignant change. What are the important lesions of the aging skin that you consider to be precancerous? How do you identify and treat actinic senile kera-

toses? One of the current fads in the United States seems to be sun-worship and sun-tanning. Is this good for oldsters? Do you tell patients in the older age groups to stay out of the sun?

DR. TRAUB: Perhaps much of the damage from the sun's rays, the wind and the weather, which Dr. Rothman mentioned, starts early in life. In other words, we should warn our patients long before they become geriatric problems that they should avoid the sun to some extent and not soak it up all day. Many sunburn preventive creams are helpful, but wind and weather on exposed parts will cause a certain amount of damage. The liklihood increases as the patient grows older.

The color of the hair is an important factor. Strangely, perhaps even more important is eye coloring. Those with fair blue eyes, or light-colored eyes, are usually much more susceptible to the sun. This is true whether the hair be blond or brunette. With graying hair, all of us are a little more susceptible to the sun than in our younger days.

As for the identification of different skin lesions seen in the old person—and they are numerous—senile keratosis is probably the most dangerous. Senile keratosis occurs mainly on exposed parts, especially the face and the back of the hand. It is a scaly, slightly inflammatory lesion which usually terminates as a prickle-cell epithelioma. In contradistinction, common seborrheic keratosis is rarely malignant. It is stated that 20 to 30 per cent of cases of senile keratosis terminate as prickle-cell epithelioma, whereas at most only 2 or 3 per cent of cases of seborrheic keratosis terminate as epithelioma (usually basal-cell).

In a skin damaged extensively by overexposure to the sun, the development of lesions is most likely and should be expected.

Cutaneous horns are usually, but not invariably, prickle-cell epithelioma at the base and should be so treated.

A patient was sent to me because lesions on his hand were thought to be warts. The lesions on his face had not been recognized. I discovered extensive colloid degeneration—for which, incidentally, little can be done.

Melanoma must not be overlooked or mistaken for deeply pigmented seborrheic keratosis, because melanoma may be highly malignant. However, in many elderly people with seborrheic keratosis, especially dark complexioned persons, a great deal of benign pigmentation may develop.

Tabs and multiple benign cystic epitheliomas around the eyes are usually of no significance and, so far as I know, do not become malignant.

Sebaceous cysts, adenomas or steatomas, are common in the elderly; they are not always benign.

Xanthelasma is always benign, and is usually seen in older people. That it may have some cardiovascular significance is open to question.

MODERATOR NELSON: Dr. Traub, tell us something about leukoplakia, the whitish thickening of the epithelium that occurs on the oral mucous membranes and the genitalia of women. How do you handle that problem? Is it important? Should we do anything about it? Why?

DR. TRAUB: I doubt whether physicians are finding this as common today as

previously. The disease is much more common in men. In the old days, we always looked upon it as due to syphilis plus tobacco. Now, it is thought that syphilis plays a minor role and that oral hygiene and perhaps the avoidance of tobacco are important. Leukoplakia should be treated conservatively and the patient kept under observation so that possible further lesions will not remain undetected. Should prickle-cell epithelioma develop, it requires immediate medical attention.

MODERATOR NELSON: What do you mean by treating it conservatively?

DR. TRAUB: I mean to discontinue smoking, put the teeth in as good condition as possible, and remove any irritation caused by the teeth. A conservative mouth wash—something as simple as salt and soda—used after meals is useful in preventing continued irritation from food particles. Some physicians believe that vitamin deficiency may be associated with leukoplakia and that vitamins, especially vitamin A, should be added to the regimen.

MODERATOR NELSON: Dr. Traub, I should also like to ask you about primary shrinkage or sclerosing atrophy of the vaginal mucosa and portions of the vulva, often seen in elderly women. This sometimes leads to stenosis of the vaginal orifice and is called kraurosis vulvae. How do you treat this, Dr. Traub? Should it be treated? Is this an atrophic process that is a precursor of cancer and, hence, important, or is it merely senile atrophy that we should forget because it is not precancerous? Gynecologists not infrequently perform vulvectomies in these patients. What is your position on that, please?

DR. TRAUB: Fortunately, this disease is rather rare. Most of the time, it is a matter of differential diagnosis. Many conditions may be mistaken for it. Itching of the vulva does not necessarily indicate kraurosis, though extensive changes together with itching and other findings may indicate the disease. These patients may also have atrophic and ulcerative lesions of the tongue, so the tongue should always be examined. The condition may be mistaken for psoriasis. Lichen sclerosus et atrophicus may also affect the vulva and should be ruled out in making a diagnosis. Some physicians believe that the changes in leukoplakia and kraurosis vulva are in the same general category.

If one can rule out the presence of all the conditions that I have mentioned, and perhaps some that in haste I have overlooked, local and conservative treatment for kraurosis is in order. If malignant change seems imminent, surgical intervention is imperative. It should be reserved for use only after thorough consultation, to be certain that all other skin ailments that might affect the vulva have been excluded.

MODERATOR NELSON: Thank you very much, Dr. Traub.

Among the most common dermatologic conditions seen in elderly people are various types of eczema involving the lower extremities. These often start as small patches, insignificant in size, which then enlarge and spread. When eczema occurs in the oldster, it is perhaps not as explosive as in younger people, but it often lasts a great deal longer. In the elderly patient we usually have the factor of stasis, and sometimes ulcers are present. Not infrequently, this low-grade stasis type of eczema harbors secondary microbial infection and then a widespread dissemination of the process takes place—a kind of autosensitization or absorption dermatitis.

These cases are difficult to manage. I shall ask Dr. Robinson to tell us how he treats a patient with stasis eczema and low-grade local infection, with perhaps an element of autosensitization. Does he think that this is related to so-called nutritional eczema in the aged? Is nutritional eczema of the lower legs in the aged a real entity, Dr. Robinson?

DR. ROBINSON: The word eczema has been used erroneously in dermatologic circles since time immemorial. Several of my confreres have tried to make changes in this nomenclature and perhaps some day someone will succeed in clarifying it. The word eczema comes from 2 Greek words which mean to "boil out." Various interpretations have been made of this diagnosis through the years, so that it has gradually become a "wastebasket" or a catch phrase to denote many types of chronic dermatitis. There is a tendency to speak of an eczematous eruption when the condition is actually allergic contact dermatitis, atopic dermatitis, an eruption caused by, or aggravated by psychogenic stimuli, or senile changes in the skin aggravated by over-zealous treatment.

We do not know how the ulcers are produced, but it is possible that some trauma may precipitate an ulcer—a break in the skin caused by striking the leg against a chair, or accidental contact with some irritating substance. An ulcer forms and secondary infection develops as a result of mishandling. The dermatitis may be a result of treatment used by the patient on the advice of well-meaning friends and neighbors or other unlicensed practitioners of medicine. We have many patients who use a variety of home remedies which include sulfur and lard, ashes, and even egg shells to treat ulcers and stasis eczema.

One of my patients had dermatitis on the feet. We discovered that the dye used in his shoe tops was the causative agent. The patient treated himself with various local applications without the advice of a physician. The lesion progressed to the stage of chronic dermatitis which some physicians call neurodermatitis. If this patient had been seen early in the course of the illness, and a steroid preparation such as hydrocortisone ointment applied locally, the chronic dermatitis might have been avoided. It is a mistake to use radiation therapy in the treatment of dermatoses on the feet of older people unless it is absolutely necessary.

The management of extensive dermatitis is probably one of the greatest problems that we are called upon to face. No two patients present the same problem, and management differs with each. The use of colloid baths is the wisest choice of therapy, if there is no evidence of secondary infection. When secondary pyogenic infection is present, an antibiotic (Neomycin) should be used.

One of the best preparations for the relief of itching in this condition is a solution of 1 per cent phenol crystals in olive oil or cottonseed oil. It would be well if we could use some of the steroid-antibiotic agents, but, if a wide surface area has to be treated, few persons can afford the cost. On small localized areas, they are valuable preparations. Possibly, with the passage of time, their cost may be reduced.

Nutritional eczema is a poor term. Senile involution of the skin sometimes results in the development of extensive erythroderma, which has been called eczema by some. In my opinion, this is not a nutritional eczema. Possibly some

elderly persons who exist on an inadequate diet, or who do not have the ability to utilize the foods ingested, may exhibit changes in the skin that are incorrectly diagnosed as eczema, but I do not like to hear that called nutritional eczema. I think the term originated during the second World War in France and other occupied countries where people were living on inadequate diets.

MODERATOR NELSON: Dr. Robinson, I take it then that, even when an old person with widespread dermatitis of the legs is in poor nutritional condition, you would not prescribe vitamins.

DR. ROBINSON: I believe that the average American citizen has an adequate diet, and therefore an adequate intake of vitamins. Adding vitamins helps little. If he has a vitamin deficiency, it is not because he does not obtain enough vitamins in his food. It is due to the fact that he is unable to utilize properly the vitamins ingested.

MODERATOR NELSON: Thank you very much, Dr. Robinson.

Another problem frequently encountered in practice is that of the elderly patient who has a contact or an irritant dermatitis which progresses and becomes very difficult to manage. In many of these cases the dermatitis, beginning on the hands or elsewhere as a rather localized eruption, spreads to other sites on the body. Once this has occurred, elimination of the contactant or irritant that caused the original condition does not seem to help, and the process of generalized eczematization continues. It often continues for a long time after the precipitating cause has been removed.

I want to ask Dr. Sulzberger how he manages such patients and what type of local therapy he uses. Does he think that the use of corticosteroids by mouth is indicated in order to break the cycle of sensitivity and autosensitization? I should like to know also, how much of a factor he thinks bacterial infection is in such cases.

Dr. Sulzberger.

DR. SULZBERGER: I should like to answer in a roundabout way the questions that Dr. Nelson has asked me. There is no firm statistical evidence, but it is the impression of practicing dermatologists with whom I have spoken (and distinctly my own impression) that contact-type allergic eczematous dermatitis is somewhat less common in the old person and in the infant than in the adolescent and the mature adult. It is interesting to speculate as to the reasons. First of all, sound experimental evidence today indicates that some acquired skin sensitivities may disappear. Thus, at a certain time of life, the load of different types of specific sensitivities that one carries reaches a peak and then is gradually diminished in old age.

It is, moreover, indisputable that exposures to contact allergens become diminished with the reduction in activity of an older person. Also, with increased experience, the older person learns to avoid exposures which he has come to recognize as harmful. In other words, not only burned children, but burned old people, dread the fire.

In addition, the immunologic mechanisms themselves are undoubtedly altered with maturation and aging. The capacity to respond with alterations, in the sense

of allergic types of changes, either becomes more effective (if you want to say it that way) or less violent (if you want to say it the other way) in the aged.

Another factor which reduces allergic reactions is that of reduced time and quantity of exposure. Perhaps because of reduction, thinning, and change in the surface film, there is less opportunity for the settling, adhesion, and cumulation of allergens, and thus less quantitative exposure of the living cells of the skin to allergens arriving from without. These allergens are sometimes soluble in the lipid film, sometimes soluble in the aqueous film, and sometimes adhere to the stratum corneum, which becomes thinned and harder in old age.

The follicles tend to atrophy and their openings often are narrowed in old age. We have now shown experimentally that these follicular openings are the main points of entrance for things penetrating the skin, so that their narrowing in old age can tend to reduce the penetration of sensitizing agents or eliciting allergens. Another important possibility is that cell susceptibilities and enzymatic pathways of older people may be transmuted by age, so that, instead of the occurrence of eczema and explosive-type reactions, certain changes in metabolism, enzymes and cellular genetics lead to carcinogenesis rather than to eczematization.

Whatever may be its cause, in contrast to what I have said about allergic eczematous reactions, a dry itchy skin is much more common in the old person than in the young. Furthermore, certain other types of eczema, but *not contact-type allergies*, are more common in the old than in the young. The eczemas of the very old are not usually contact allergies. Nummular eczema, which is more common after middle-age and in the elderly, is not a contact-type allergy.

In answer to your question, I think that micro-organisms generally play some role. Moreover, in nummular eczema, the work done by H. Storck in Zurich may have some bearing on this problem. He showed that, when a culture is made of material taken from the skin surface of people with certain eczemas, then an extract is made of the culture, and the extract is applied to the skin of these people, the specific type of eczema is reproduced. It is not reproduced when cultures are taken from the skins of other persons, nor is this type of eczema produced in persons who do not have nummular eczema.

In reply to another of your questions, Dr. Nelson, I am convinced that if prescribed properly and judiciously, with full awareness of dangers and contraindications, and when used only after all possible examinations have been fulfilled to rule contraindications, systemically administered corticosteroids and perhaps even ACTH can be used to break the vicious cycle of itching, in carefully selected cases.

I should like to say a word about the reason for the dryness and itching of senile skin as we see it today. Everyone agrees that there is loss of the capacity of the skin for hydration. I say skin, meaning the whole skin. This occurs in the dermis due to the reduced hydration capacity of the collagen and ground substance, and it has been shown, or postulated, to exist in the horny layer. As we know from the work of Irving Blank, the nonhydrated horny layer is brittle, scales, and breaks off, whereas the properly hydrated horny layer takes up a certain amount of water and becomes pliable. It appears quite likely that the

proteins, lipids and other chemicals in the horny layer of the skin of old people will take up and hold water less well than the horny layer at younger ages.

The question that has always been in my mind is whether or not it is illogical to use estrogens in order to increase both the oil and the size of the oil glands of the human skin in an attempt to counteract the effects of atrophy in aging. It might be more logical—and here much experimentation is required—to use androgens or progesterone, *i.e.*, anabolic substances, to increase the sebaceous secretion and activity. In addition, in order to increase plumping and water retention, it might be interesting and perhaps profitable to try the local application of such water-retaining steroids as fluorhydrocortisone and aldosterone instead of estrogens.

MODERATOR NELSON: You are making the point, Dr. Sulzberger, that if you want to hydrate an old skin and make it pliable, you would soak that skin or hydrate it before applying an occlusive or oily substance. Is that true?

DR. SULZBERGER: That is only partially true. I wish one could do that, Dr. Nelson, but the point is that when you immerse the skin in the bath, you start to hydrate a given horny layer which is capable of taking up a certain amount of water. However, in the old person the horny layer in all probability is inherently incapable of holding the amount of water that it should, because of its chemical constitution. Thus, immersion in water is a two-edged sword; although it hydrates temporarily, it probably also leaches out the very substances needed by the horny layer to permit it to retain water.

I should like to have Dr. Rothman speak on this question, to see whether or not he agrees with me. At any rate, bathing may provide temporary relief, even when the skin is greased. Eventually, however, it may become harmful and cause further drying out—for instance, the effect of water in producing chapping. Chapping is a simple example of the production of excessive dryness and inflammation due to water, detergents and cold, in the young as well as in the old.

Certain things will decrease the hydration capacity of collagen. Among them are certain metallic salts. Franz Herrmann, as long ago as 1930, showed that one kind of salts (calcium), known to be increased in the skin of the elderly, actually decreases the capacity of the colloidal systems to hold water.

Many avenues appear for fruitful research studies in dermato-geriatrics. Despite the 150 years of experience that this panel represents and the perhaps 1,500,000 combined years of experience on the part of dermatologists throughout the world, little basic research has yet been carried out on the physiology and functions of the skin, on the changes in old age, on the chemistry of the skin's surface film rather than of its deeper structures, and on the way in which the skin's chemical constituents and physiologic functions can be altered under the influence of modern medicinal preparations at our command. Little work has been done using modern techniques of study, such as modern biochemistry, biophysics, and electrophysics, before and after the application of modern methods of treatment to the skin. It is a most promising and challenging field, and I think it would be a most rewarding one.

Before I close, I should like to say something about the incidence of carcinoma,

and how important skin cancer is numerically. According to figures compiled by Heller of the United States Public Health Service and published at the end of 1955, 328.0 cases of cancer were reported per 100,000 of the population. Of these, 40.4 were cancers of the skin, a larger number than for any other organ—for example, only 36.0 were cancers of the breast. If carcinomas of the skin and the lip (usually seen by the dermatologist) are included, the number becomes 45 per 100,000 of the population—more than for any other organ. This reported incidence of skin cancers must be far too low a figure, because most cutaneous cancers are destroyed, removed, or cured by dermatologists without coming to a general pathologic laboratory and without ever being reported. Heller's figures would probably have to be multiplied by a large factor in order to obtain the true incidence. The incidence of skin cancer is highest in the white male. When the Negro and the female are eliminated, cancer of the skin becomes even more important numerically.

The mortality rate for cancer of the skin is much higher than one would suppose, though it is lower than the mortality rate for hidden cancers, which cannot be discovered early. Nevertheless, 2.4 is not a negligible mortality rate. The mortality rate for cancer of the skin exceeds that for carcinoma of the kidney, brain, larynx, pharynx and tongue. The figures were astonishing to me when I first saw them.

The change in senile skin which leads to flattening of the epithelium is accompanied by an increase in the number of mitoses—which seems to be a paradox. Nevertheless, the fact that mitotic activity is increased although there is simultaneous atrophy, suggests that carcinogenic exposures and irritants of various kinds may find unusually fertile soil for producing malignant changes. This is indeed the case, as we know both from clinical observations and from results of experiments in laboratory animals of different ages.

MODERATOR NELSON: Thank you very much, Dr. Sulzberger.

I should like to open this discussion to members of the audience so that they may ask any questions that they wish.

QUESTION FROM THE AUDIENCE: I should like to ask two questions: 1) Does the base for cortisone ointment present any particular problem? Some ointments have a petrolatum base, some contain mineral oil, and others have a water-miscible base. Is any base suitable for a cortisone ointment? Does any one of them suffice? 2) Comment was made on sun-worshiping by the elderly person. How much damage does the sun do to the skin of elderly people? Apparently, it is not enough to disrupt the Florida trade.

MODERATOR NELSON: Who would like to answer the first question? "Does the base used in corticosteroid ointments really matter?"

DR. ROBINSON: I believe that the simplest possible base is the best. In our original investigative work, we used a simple hydrocarbon base, containing one-third mineral oil and two-thirds petrolatum. We had the lowest incidence of reactions while using such a preparation. Recently, the commercial ointments with an oily base have contained lanolin. I think the choice of base depends upon the area being treated. If the skin is exceptionally dry, one should not use a drying

agent, such as a lotion base or a greaseless base. In that instance, and particularly in the aged, oily vehicles are far superior.

MODERATOR NELSON: Would everyone on the panel agree that a greasy base for steroid ointments would be indicated in old people?

Dr. Rein?

DR. REIN: Two points should be mentioned: First, we have yet to find a patient sensitive to the steroid itself. Persons who react unfavorably to the cortisone preparation usually do so because of the base. Second, the selection of the type of base depends upon the location of the lesion and the type of skin involved. When you are dealing with a very dry skin, oily bases are better. This is particularly true around the face. If you are dealing with the skin of the groins and areas where there is maceration and sweating, lotions are far superior. The choice of preparation would depend to a large extent upon the status of the condition, the amount of dryness, and the area involved.

MODERATOR NELSON: Thank you. Dr. Sulzberger, have you a comment?

DR. SULZBERGER: In our careful and extensive comparisons of the same active ingredients in different bases, we have found that it is difficult to set up a rule for predicting which base will prove best for a given dermatosis or a given site, in a particular person. As an example, let us take symmetrically situated lesions treated with, let us say, hydrocortisone free-alcohol in a petrolatum base compared with hydrocortisone in a watery cream. Some patients will respond well on the side treated with the watery cream but not on the other side treated with the petrolatum-base preparation; and some patients will respond in exactly the opposite way.

In general, simple petrolatum bases are less irritating and better tolerated. Lotions have certain advantages because they are economical to use. Better and more widespread application of a small amount of hydrocortisone can be secured with a lotion, because larger skin areas can be covered rapidly with a thin film that can be rubbed in. Therefore, it is often cheaper for a patient with an extensive dermatosis to use hydrocortisone in a lotion vehicle.

The question of sensitization is important. As far as I know, no case of proved sensitization to hydrocortisone has come to light. All the cases reported as hypersensitivity presumed to be due to hydrocortisone have been shown to be due either to the base itself (not to petrolatum but to the other ingredients of bases) or to the admixture of other substances, such as antibiotics, tars or quinolines.

MODERATOR NELSON: Thank you very much. I think Dr. Traub should answer the second question. "What damage does the sun do to the skin of the aged?" It has been pointed out that possible damage from the sun does not affect the Florida trade.

DR. TRAUB: The one established and well recognized causative factor in skin cancer is the sun. The incidence of cutaneous cancer is so high in the southwestern parts of the United States, that it is beyond doubt that the sun plays a decided role.

I am not at all certain that the effect of the sun is worse after a certain age. It may not be. Dr. Sulzberger mentioned that the skin of the older person is

not so subject to allergies. Perhaps, at some point, the oldster can take a certain extra amount of sun that would have an adverse effect at an earlier age.

My impression is that probably most old people do not lie all day long in the sun as so many youngsters do. If cutaneous malignancy develops, it does so over a long period of time, and not suddenly when the patient has retired and gone to Florida. It is a slow process. Perhaps the old person's skin is quite tolerant to the sun. Nevertheless, the sun is a great factor in the production of cutaneous cancer. There is no question about that.

MODERATOR NELSON: Dr. Rothman, would you like to say something?

DR. ROTHMAN: I should like to amplify what Dr. Traub has said. The United States Public Health statistics have divided the United States into 3 latitudes—north, middle, and southern. The occurrence of skin and lip cancer is twenty times greater in the southern third than in the northern third. We know that it is relatively easy to elicit cancers of the skin in experimental animals with ultraviolet light. Furthermore, we know the wavelengths that have this effect. As for the specific question as to whether or not old people really are harmed by sunshine, I am talking rather about chronic exposure which starts long before senescence. People so exposed usually have so-called sailor's skin or farmer's skin, characterized by multiple keratosis and carcinomata of the face and hands. These persons usually commence exposure to sunshine early in youth. Then, when they are 50 or 60 years of age, they suffer from skin cancer. I agree that it won't hurt old people to sit out and get a little warm sunshine, particularly if they do not sit for hours and hours.

MODERATOR NELSON: Thank you very much.

DR. TRAUB: I should like to emphasize that point again, because there is an erroneous opinion among people that sunburn predisposes to cancer. That is not true. It is chronic exposure over long periods of time. People who go to Florida for two or three weeks are not the ones in whom cancer develops. They go down there and acquire a tan because they want to impress their friends by going to Florida for a vacation. I do not think it will affect the Florida traffic or income. However, a mistake frequently made is for the general practitioner to advise older patients to buy a sun lamp and use it at home. Sun lamps have done more harm than good because of indiscriminate use over long periods of time.

DR. ROTHMAN: There is one more thing. We have spoken about the drying of old skin, which is much worse in winter, and causes pruritus. Dryness will grow worse with the use of an ultraviolet lamp. I oppose their use.

If I may discuss some of the other panel members' remarks about pruritus and dry, scaly skin in the aged—in my experience, the treatment is rather simple, if you put on a little bit of grease. In most cases, it will not be necessary to give steroids or antihistamines internally. Simple greasing and restriction of water and soap is a most effective treatment.

MODERATOR NELSON: Do antihistamines do any good?

DR. ROTHMAN: I would be opposed to what Dr. Rein said about using antihistamines for the sake of a side-effect. Antihistamines are for neutralizing histamine. If I want sedation, I do not give Benadryl, but give phenobarbital.

DR. REIN: I should like to ask Dr. Rothman whether or not he believes that it is safer to give phenobarbital than one of the other preparations in elderly people.

DR. ROTHMAN: I think phenobarbital is much safer.

QUESTION FROM THE AUDIENCE: How frequently are two different types of skin cancer found in the same person?

DR. TRAUB: I shall try to answer that. I cannot give exact figures, but a person who has multiple basal-cell epitheliomas on the trunk that remain any length of time may often also have a prickle-cell epithelioma. We may see a prickle-cell epithelioma on the lip in a patient who has multiple basal-cell epitheliomas on the face. For instance, I have had quite a number of patients of Irish extraction with fair skin and blue eyes, who have had from 50 to 70 or more lesions of various types on the face. Some of these lesions were prickle-cell and some were basal-cell epitheliomas. This combination is not at all uncommon.

MODERATOR NELSON: I have several prospective questions from the audience.

QUESTION FROM THE AUDIENCE: Is there any advantage in the use of androgen-estrogen combinations in the management of the senile skin or of changes dependent upon old age?

DR. SULZBERGER: I shall try to answer. By and large, the results of administration of these hormones have been disappointing. For a long time there was a vogue for giving testosterone to old men with pruritus. Sometimes it helped them in other ways, but not usually with their itching.

MODERATOR NELSON: Another question?

SPEAKER FROM THE AUDIENCE: Many companies have marketed androgen-estrogen products. The reports by men in that field claim good results.

MODERATOR NELSON: In other words, "Why does the panel disagree with the reports those drug salesmen show you?"

DR. SULZBERGER: That is a fair question. You should not take one man's opinion. What is the experience of the other members of this panel with regard to the value of estrogens and androgens in pruritus in the aged?

MODERATOR NELSON: Dr. Rothman?

DR. ROTHMAN: My answer is that they are no good. A little greasing does much better.

MODERATOR NELSON: Dr. Traub?

DR. TRAUB: I agree with Dr. Rothman. Out West, where I come from, they used to sew everyone into red flannels after applying goose grease. I don't remember seeing much senile pruritus or winter pruritus then.

MODERATOR NELSON: Another question?

SPEAKER FROM THE AUDIENCE: I should like to ask the panelists what they think of the use of royal jelly from bees in the local treatment of "geriatric" skin.

DR. SULZBERGER: I think the users get stung!

SPEAKER FROM THE AUDIENCE: I should like to know whether or not anything can be taken internally to help prevent dryness of the skin.

MODERATOR NELSON: "Can anything be taken internally to prevent dryness

of the skin?" Presumably this refers to substances other than androgens and estrogens.

DR. ROTHMAN: No, nothing can be taken for that purpose. Diets with excessive fat or carbohydrate intakes have not increased the supply of oil to the horny layer.

QUESTION FROM THE AUDIENCE: Is there any correlation between low thyroid activity in the elderly and the prevalence of dry skin?

MODERATOR NELSON: I take it that the questioner is not referring to straightforward myxedema. Does anyone on the panel want to answer the question?

DR. SULZBERGER: That is a good question. The answer is that, in pruritus of the aged, one does not find thyroid dysfunction uniformly. Small doses of thyroid have not been particularly helpful. You must remember that there are certain isolated cases in which these things help. Even estrogens and androgens help in some cases. Thyroid helps in some cases, but not in general. Such a thing as triiodothyronine, locally or even systemically, is worthy of further trial in the treatment of trophic disturbances of the aged skin, but has not yet proved its superiority in our hands.

SPEAKER FROM THE AUDIENCE: Vitamin A is commonly used for its effect upon the membranes of the nose, the eyes, and the ears. Dr. Sulzberger has warned against the use of too much vitamin A. My first question is: At what point should we stop giving vitamin A? Dosages of from 100,000 to 150,000 units per day have been used without side-effects.

We should also like to receive aid from dermatologists in our health examinations. What can you tell us about the skin that would give us information concerning the circulatory system, the heart, and so on? Dr. Conrad Berens says that 32 different systemic diseases can be manifested and recognized in the eye. What can we say with regard to the skin?

MODERATOR NELSON: The first question was, "What is too much vitamin A?" As Dr. Sulzberger is the expert on excessive intake of vitamin A, I shall ask him to answer the question.

DR. SULZBERGER: Manifest hypervitaminosis A in the adult is extremely rare, despite large doses. Nevertheless, as a measure of caution, if one gives as much as 50,000 to 150,000 units or more a day, treatment should be interrupted. I let my patients take such doses for three months and then give them a month of rest in which the liver and other depots can clear. That is a simple approach.

Probably not more than a dozen cases of hypervitaminosis A in the adult have been reported since M. Paul Lazar and I reported the first case. An excellent study and review of this whole subject was recently published by Roger C. Breslau (*Arch. Pediat.* **74:** 139 (Apr.) 1957, and **74:** 178 (May) 1957). Although the tendency toward ill effects is great in children, it is almost negligible in adults. Moreover, the effect of administration of vitamin A in these large doses is quite erratic. In many patients, it is not possible to raise the blood level even with huge doses. We have been studying this for a long time. For some reason, high levels are reached quickly in some patients and not in others.

QUESTION FROM THE AUDIENCE: I should like to ask Dr. Sulzberger whether or not clinical effects are obtained in the adult and in the elderly by giving vitamin A. Is the skin changed?

DR. SULZBERGER: In some isolated cases, the skin and nails are improved, and become less dry and brittle.

MODERATOR NELSON: It is rather an expensive form of treatment. Do you think it is justified in elderly people?

DR. SULZBERGER: As a general rule, it is not. In a large series of cases of acne and other dermatoses, we administered as much as 150,000 units of vitamin A daily for prolonged periods and could find no consistent elevations in the blood levels, nor could we correlate any of the clinical cutaneous changes that occurred in these patients, either for better or worse, with the blood levels of vitamin A.

MODERATOR NELSON: Was this acne in the aged?

DR. SULZBERGER: No. We were treating ordinary juvenile acne, and it was a matter of studying the vitamin A levels. Using the concentration in the blood stream as a criterion, one cannot demonstrate any correlation with clinical changes, nor evaluate what vitamin A does. I often wonder whether it does anything.

MODERATOR NELSON: Who would like to answer the second question, "What help can the dermatologist give to the internist in the general physical examination?"

By default, I may answer that question myself. The practiced eye can probably recognize the manifestations of more than 32 different internal diseases in the skin. Our position at the Presbyterian Hospital is that the field of dermatology includes the skin and everything that it encases.

QUESTION FROM THE AUDIENCE: I should like to ask the panelists about conditions such as lupus erythematosus and scleroderma, which formerly were considered to be chronic diseases with purely dermatologic manifestations, but now are known to be widespread throughout the body. The incidence of these diseases seems to be increasing, or at least they now seem to be recognized with greater frequency. Is this increase real, or is it only relative?

DR. REIN: Our diagnostic methods are becoming better and our awareness of these diseases is greater. Better recognition probably accounts for much of the apparent increase. However, lupus erythematosus is not a problem of the aged.

DR. SULZBERGER: I should like to correct one impression. It was the nondermatologists who thought that these diseases were confined to the skin. Dermatologists never thought so. Ever since the first descriptions of Hebra appeared, it has been known by dermatologists that the viscera are involved in such conditions as systemic lupus erythematosus or sclerodactylia. The same thing applies to such a disease as sarcoid. In fact, dermatologists elucidated the localizations in internal organs and noncutaneous organs long before internists knew that these entities were anything but difficult and irritating names.

MODERATOR NELSON: I think that is true. Internists are now discovering some dermatologic diseases that these panelists have known for a long time. For

example, Stevens-Johnson syndrome became a watchword in 1922 for a condition that had been adequately described in dermatologic literature since 1878.

DR. ROBINSON: May I say something about Stevens-Johnson disease? That is a very sore point with me because that was one of the poorest papers ever to appear in medical literature. The disease was called eruptive fever with ophthalmia and 2 patients reported, but one had no fever and the other had no ophthalmia. The condition is really a type of severe erythema multiforme.

QUESTION FROM THE AUDIENCE: May I ask the panelists about their experience with industrial dermatoses and malignancy due to the use of cutting oils? Is there any relation between exposure to cutting oils and carcinoma of the skin?

MODERATOR NELSON: Dr. Traub, please.

DR. TRAUB: During the war, we made some studies on that question, but we did not find any cases in which cutting oil caused a cutaneous cancer. We did see a considerable number of cases of pyoderma. People who work in tar fields frequently have cutaneous carcinomas. I know of one factory where both basal-cell and prickle-cell lesions occurred at a rapid rate. So far as I am aware, these lesions are not caused by cutting oils.

MODERATOR NELSON: Are there other questions?

QUESTION FROM THE AUDIENCE: What do you think about enzyme treatment for ulceration of an extremity?

MODERATOR NELSON: The question was, "What is the value of enzyme treatment in leg ulcers?"

DR ROBINSON: Enzymes such as streptodornase and streptokinase have been used topically with some alleged success in the treatment of leg ulcers.

MODERATOR NELSON: Dr. Rothman, do you use this type of treatment?

DR. ROTHMAN: No, I don't. One can fare well without it.

SPEAKER FROM THE AUDIENCE: Dr. Nelson, in behalf of all in the audience, I want to thank you and your panel for a fine presentation.

DR. LAURANCE W. KINSELL, presiding: Speaking for any other internists who may be here, I feel properly in my place and will ask the dermatologists to assist me in diagnosis. The old dictum, "Know syphilis and you know medicine," perhaps is not quite so apropos as it used to be when syphilis was more rampant, but certainly, "Know the skin and you know diagnosis," is still a good one.

CURRENT CONCEPTS IN THE MANAGEMENT OF OSTEOPOROSIS

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INTRODUCTION

Osteoporosis is not only the most widespread metabolic disease of bone, but also the common denominator in a wide variety of disorders which may have no similar or closely related disturbance of structure or function. An understanding of normal bone metabolism and the pathologic physiology underlying osteoporotic manifestations is necessary in order to appreciate the principles of treatment.

Normal bone

The osseous mass is a living system, constantly in flux and subject to hormonal influences. It undergoes continuously processes of appositional growth, resorption, and remodeling. Bone consists of specialized connective tissue in which the intercellular substance is impregnated with lime salts. This intercellular substance, bone matrix or osteoid, has as its major component a protein polypeptide. The mineral salts are principally calcium carbonate-phosphates, serving as a lattice or internal scaffolding on which is deposited a mantle of adventitious inorganic substances. Specialized cells, the osteoblasts and osteoclasts, are concerned with bone production and resorption, respectively. The mineral composition of bone varies in different persons of identical age and sex (1). It also varies at different times and in different bones within the same person, reflecting the qualitative and quantitative changes in the biologic fluids surrounding osseous tissue.

There is variance of opinion concerning the physical relationship of the bone matrix to the mineral salts (2). Either the protein-carbohydrate moieties combine with the minerals to form an undissociable complex, or the bone matrix merely provides an architectural template for the crystals of bone salt. Leaching of the mineral phase from calcified matrix induces an alteration in the physical state of its organic components, modifying its capacity to undergo calcification. Much of the sequential pattern in the formation and resorption of normal bone is conjectural. The interplay of many hormonal and nutritive agents also awaits elucidation.

CLINICAL CONSIDERATIONS

Pathogenesis of osteoporosis

The accepted fundamental etiologic disturbance in osteoporosis is defective osteogenesis or, more explicitly, faulty matrix formation. An important distinction is between osteoporosis on the one hand, and osteomalacia and osteitis fibrosa generalisata on the other. The latter 2 conditions also fall into the prov-

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ince of insufficiently calcified bone, but here the first is due to defective matrix calcification, and the second to excessive resorption. Differential chemical findings in these 3 conditions and other derangements characterized by rarefied bone (such as osteitis deformans, or multiple myeloma) have been tabulated by Reifenstein (3). Cognizance of these features is mandatory inasmuch as the therapeutic approach varies in each case. Decreased density of bone on the x-ray film may represent any of the aforementioned conditions. This is particularly significant concerning recognition of early phases of disease, since it may be impossible to detect changes in density with accuracy until almost 30 per cent demineralization has occurred (4).

Weight is lent to the observation that the bone matrix is at fault in osteoporosis by the normal concentrations of serum calcium and phosphorus. This concept, that the principal aberration lies in the mechanism of matrix formation, whereas the mineral metabolism disturbance is an ancillary feature, merits emphasis. Hypercalciuria, when present, is associated only with rapidly developing osteoporosis, a condition in which osteolysis exceeds whatever osteogenesis is taking place. Contrariwise, in long-standing osteoporosis, the excretion of calcium (as estimated by the Sulkowitch test) is within normal limits. Presumably, depletion of the skeleton progresses just to the extent of stimulating osteoblastic activity, and this compensatory response prevents such discrepancy between bone formation and resorption as might lead to hypercalciuria (3). This same postulation accounts for the normal level of the index of osteoblastic activity—serum alkaline phosphatase (5, 6). It should be kept in mind that serum protein values do not necessarily reflect the true picture of bone and tissue protein. In the final analysis, although the net bone mass in long-standing osteoporosis uncomplicated by other bone disease is diminished, alterations detectable by laboratory determinations are usually lacking.

Diagnostic features

One needs hardly to be reminded that the first step in diagnosis must cover the ground encompassed in every thorough initial examination. A painstaking and meticulous history and physical survey, appropriate laboratory studies, and such additional special procedures as may be suggested are prerequisites.

Use of the roentgen ray is obligatory, but reliance on it must be tempered by a recognition of its limitations. Unfortunately, only incomplete and sometimes deceptive information is obtained thereby; individual cases show considerable diversity (7, 8), and clinical manifestations frequently do not parallel the radiologic appearance of the skeleton. As has been inferred already, only the passage of time discloses organic disease not demonstrable previously. Moreover, with scattered exceptions (9, 10), most physicians assert that subsidence of symptoms as the result of successful treatment is not necessarily correlated or synchronous with improvement in the roentgenographic data. These serious shortcomings notwithstanding, roentgen examination is still the cornerstone on which the correct diagnosis is erected. "Typical" radiographic findings in osteoporosis are reviewed in Table 1.

A note of caution should be injected concerning the too frequent use of roent-

TABLE 1

Principal Features of Osteoporosis

Etiopathogenesis	Decreased osteoblastic activity, and/or defective bone matrix. Hyperparathyroidism absent.
History	Easy fatigability, gradual rounding of shoulders, inability to stand erect. Incapacitation, kyphoscoliosis and stooped posture progressive. Spontaneous excruciating pain initiated by trivial injury.
Signs and symptoms	Persistent pain throughout entire spine, but mainly in dorsal region, frequently radiating around chest wall or pelvis (girdle distribution) and aggravated by physical exertion. Skeletal deformities. Psoas and other muscle spasm and atrophy. Point tenderness over involved vertebrae. Considerable articular limitation of spine.
Laboratory findings	Serum calcium, inorganic phosphorus, and alkaline phosphatase concentrations within normal limits. Low-normal level of total serum protein, with normal A/G ratio. Non-specific secondary anemia. No blood acidosis. Urinary calcium normal or slightly increased.
Radiologic characteristics	Marked rarefaction of bone structure. Predilection for spine and pelvis. "Codfish" vertebrae. Biconcave compressions and flattening in lumbar region, and wedging in dorsal spine. Marked thinning of compact layer of bones. Poor osseous trabeculae. Pathologic fractures present, the vertebrae and femoral neck being particularly susceptible sites.

genography in the diagnosis of osteoporosis, or in the unfounded expectation of following thereby the beneficial effects of therapy. Osteoporosis may be caused by direct damage to osteoblasts from irradiation, whether it be x-ray activity or radioactivity (11, 12). There are reports of osteoporosis and fracture as sequelae several months after pelvic radiotherapy (13, 14). Although there are no satisfactory criteria for appraising the cumulative effects of diagnostic x-ray irradiation on bone, it would seem wise, in the light of these reports, to employ roentgenography as sparingly as possible.

Very high frequency beams may also cause destruction of bone. Ultrasonoscopy is being used increasingly in diathermy, for discovering tumors, and in the treatment of certain neuralgias and malignant lesions. With the widespread use of this modality, one may expect to find in the future a greater incidence of osteoporosis induced inadvertently by its careless application.

Biopsy of bone has been employed for diagnostic purposes and to ascertain the efficacy of treatment. Schüpbach (15) and Sherman (9) reported various histologic changes denoting improvement of the bone morphology after a favorable course of therapy. The routine use of serial bone biopsies is not feasible clinically, however, at the present time.

Again, the condition of the teeth and jaws may yield information. Cahn (16), and Groen and his associates (17) reported paradentosis as a sign in the osteoporosis of ovarian insufficiency. The lamina dura about the teeth is intact in osteoporosis—a significant factor in its radiologic differentiation from osteitis fibrosa generalisata (5).

Available reports are too fragmentary to enable assessment of the so-called

"calcium tolerance test," which has been proposed as an easy screening procedure for detecting early osteoporosis and promoting prophylactic or therapeutic measures (18–20).

Causes of osteoporosis

A provisional classification of the causes of osteoporosis, which embodies most conditions in which this disorder may become manifest, has been compiled by the authors and is listed in Table 2. Whatever the cause, the end-effect of de-

TABLE 2

Classification of Causes of Osteoporosis

I. *Disturbance in Osteoblastic Activity*
  A. Atrophy of disuse
    Loss of stress and strain on skeleton as a result of
    1) Immobilization: Fractures, osteoarticular tuberculosis
    2) Paralysis of muscles pulling on skeleton:
      Poliomyelitis, paraplegia
  B. Hypoestrinism
    1) Congenital: Ovarian agenesis
    2) Acquired: Castration
      Infections
    3) Functional: Postmenopausal (before 65)
      Senile (after 65)
  C. Congenital osteoblastic defect
    Osteogenesis imperfecta (fragilitas ossium)
II. *Disturbance in Matrix*
  A. Absolute or relative inadequacy of nitrogenous components
    1) Decreased intake: Malnutrition, anorexia nervosa
    2) Increased breakdown: Hyperthyroidism, diabetes mellitus
    3) Malabsorption or deficient utilization: Hepatic, pancreatic, and/or gastrointestinal disease, *e.g.*, sprue
    4) Excessive loss: Nephrosis, extensive burns
  B. Inability to retain or form matrix from nitrogenous components
    1) Androgen deficiency: Eunuchoidism
      Castration
      Infections
      Senility
    2) Hypovitaminosis C
    3) Excess cortisone-like substances:
      Prolonged stress ("alarm reaction")
      Cortisone and ACTH therapy
      Adrenal hypercorticalism (Cushing's syndrome)
III. *Disturbance in both Matrix and Osteoblasts*
  A. Destruction
    Irradiation
    Ultrasonic waves
  B. Post-traumatic
    Sudeck's atrophy
IV. *Defect Unknown*
  A. "Idiopathic"
  B. Acromegaly

ficient matrix is the same in the bone area involved. It is commonplace for 2 or more of these circumstances to coexist in the same patient. To illustrate: severe osteoporosis may be evident postoperatively in an elderly woman due to the summation of immobilization, impaired appetite, and the metabolic response to surgery superimposed on postmenopausal changes.

Clinical manifestations of osteoporosis

Regardless of the etiologic type, the symptomatic consequences of osteoporosis are comparable qualitatively, within certain limits. It is obvious that, since a number of entities may contribute jointly to the presenting clinical picture, certain features in the latter can be imputed to variants other than the osteoporosis itself. The correct approach to the management of osteoporosis is to view the problem in its entire breadth, extracting each possible causative factor, and thereby attempting to treat the patient's complaints on a more rational basis.

In many cases, osteoporosis remains asymptomatic (21), or is ushered in by only vague and mild skeletal pains and weakness. In other cases the process follows a protracted course and leads progressively to crippling, deterioration of health and, barring effective treatment, ultimately to total invalidism. The usual symptomatology, as set forth in Table 1, applies most closely to postmenopausal osteoporosis, but many facets of it may be seen concomitantly in any of the other types. The clinical picture has been amplified by other authors (22–24).

The pattern of the pain maps out the major bone regions which show a predilection for osteoporosis, *viz*, the spine, ribs and pelvis. The skull and extremities are usually spared, this fact being of paramount importance in helping to differentiate osteoporosis from other decalcifying bone diseases. Exceptions are seen in partial immobilization and traumatic osteoporosis, in which rarefaction is confined to the involved extremity. The relative freedom from infringement of the calvarium in osteoporosis has been attributed to continuing stresses, of necessity placed on the head, from such obligatory functions as mastication, deglutition, speech or facial expression, regardless of the degree of inactivity of the remainder of the axial and appendicular skeleton (5, 25). This explanation is not tenable in the case of Schüller's disease (osteoporosis circumscripta cranii), a distinctive type of osteoporosis wherein the lesions appear to be limited exclusively to the skull.

Baker (26) cautions against glibly ascribing pain in the back to osteoporosis. Even if the suspicion of osteoporosis is substantiated, one must rule out any possible coexistent visceral component of such pain—for instance, that due to pancreatic carcinoma or to ulceration of the posterior wall of the stomach.

MANAGEMENT OF OSTEOPOROSIS

The cardinal objectives of treatment in osteoporosis are dictated by a dual purpose—remedy of all underlying causative factors, and enhancement of osteoblastic function in a healthy bone matrix. The definitive management is concerned with alleviating pain, restoring the structure of the bones, and preventing further deformity.

Although the significance of many of the general principles concerned with the mechanism of osteoporosis may be clear, the precise application of these principles in the elucidation of osteoporosis as it appears in specific clinical conditions is not always possible. Bearing in mind that the primary goal of treatment is correction of the disease entity of which osteoporosis may be a feature, it does not become necessary to consider each of these particular entities in detail. Rather they will be surveyed in a cursory manner as the various approaches in the management of osteoporosis are discussed.

Mobilization and exercise

"As the strength of wood is a function of wind resistance, so the strength of bone is a function of stress (25)."

The major stimulus for osteoblastic activity consists of the multitudinous stresses and strains to which the skeleton is subjected under ordinary normal circumstances. Prolonged or extensive immobilization of a formerly active portion of the body inhibits this all-important stimulus to osteogenesis (27). Bone resorption continues unabated, however, and the end-result is osteoporosis, the so-called atrophy of disuse (28, 29). A patient may be lamed more by this eventual osteoporosis than he might have been had his injured extremity been kept active.

Deitrick, Whedon and Shorr (30, 31) reaffirmed the views of earlier investigators (27, 32–38) and showed that, with immobilization, a person incurs a large protein deficit and metabolic derangements. While the wear and tear on mature osteoid continues in the interim, there is no disturbance of mineralization of whatever matrix is present (39). The deficiency is in the deposit of new protein bone matrix. Various types of osteoporosis, however, may demonstrate a net loss of half to two-thirds of the total body minerals (40).

Atrophy of disuse occurs in severely bedfast patients, such as those in whom serious fractures necessitate extensive encasement in plaster. There appears to be no important difference between immobilization as such and injury followed by immobilization (41). It is acknowledged that the extent of osteoporosis is directly proportional to the thoroughness of immobilization. Furthermore, osteoporosis is far more acute when due to disuse atrophy than when due to other conditions, and therefore electrolyte alterations become evident, and urinary calcium excretion increases. Hence the propensity for renal stones (42–45). This presents certain problems with reference to diet.

Increased calcium intake augments intestinal absorption of this mineral, thereby facilitating the development of calculi in the nonambulant patient. The same situation applies to excessive ingestion of vitamin D, since it increases the absorption of calcium from the alimentary tract. Accordingly, it may be wise to curtail the intake of these substances in the immobilized patient, particularly the older person with impaired renal function—just enough being allowed to maintain a positive calcium balance and so counteract the tendency to mechanical collapse of osteoporotic cancellous bone (46). In a certain military hospital, liberal consumption of milk is thought to have been the cause of renal stones in

7 per cent of patients with fracture of the femoral shaft, a type of fracture which otherwise rarely gives rise to urinary lithiasis (47).

The younger the patient, the more severe the consequences of immobilization (48). Not only hypercalciuria, but also hypercalcemia and hyperphosphatemia can develop. Stasis exists already. The danger of ectopic soft-tissue calcification, particularly of the kidneys, is thus evoked. Diffuse deposition of calcium in the renal parenchyma may give rise to nephrocalcinosis, oliguria, and uremia (49). With the onset of disturbances of this sort, mobilization is imperative if the patient is to survive, irrespective of the condition necessitating immobilization originally (5, 50–52). These complications may be avoided by employing as yardsticks the specific gravity of the morning urine throughout the immobilization period, and the level of serum calcium, as recommended by Halvorsen (48) and Wakefield (53). One should be alert to the possibility of hypercalcemia when anorexia, nausea, asthenia, and polyuria develop (54).

To Deitrick and his associates (55, 56) goes the credit for first employing the Sanders motorized oscillating bed (57) as an aid in overcoming the ill-effects provoked by long-term immobilization (58). Dommisse and Nangle (59) constructed a pulley-and-rope apparatus, for attachment to orthopedic casts, which permitted easy maneuverability of the patient's body in many directions. These authors reported that the device gave maximal mobility with comfort in bed, that its use diminished muscular wasting and decubitus ulceration, and facilitated postural drainage of the renal pelvis. Experience with this appliance is limited, to date.

A practice that is mentioned only to be condemned is the indiscriminate use of plaster jackets or corsets under circumstances in which the patient would fare better with conscientiously applied exercises. A tenet of sound contemporary orthopedic rehabilitation is early ambulation, and the instruction of patients in developing strong muscle tone. The uncalled-for use of spinal braces and such paraphernalia is a hazardous undertaking that only too frequently abets muscular atrophy. It is not uncommon for a physician who has become alarmed by the patient's roentgen findings, to err and unwittingly prescribe immobilization in bed.

In recent years the concept of a role for neurotrophic influences in bone formation has been resurrected (60). These stimuli are said to maintain the normal composition of bone, and their absence is presumably the cause of atrophy. The importance of the part played by cessation of neurotrophic factors in immobilization is open to speculation (47).

Dietary considerations: protein, fluids, minerals and vitamins

Osteoporosis has been regarded by various authors as being due primarily to a generalized nutritional disturbance (61–66). Alwens (67) cited the sudden occurrence of osteoporosis, because of wartime famine, in a part of Austria where this syndrome had been rarely observed previously. The condition affected large numbers of persons of all ages from 19 to 72. The hypothesis of a systemic dietetic deficiency has been held in disfavor by most clinicians in this country, where the

hormonal school has its staunchest proponents. In the aged, defective alimentation, gastro-intestinal dysfunction, and insufficiency of the glandular apparatus seem so intricately interlinked that a pattern of causality cannot possibly be established.

Despite the ambiguity which continues to enshroud this subject, an incontestable fact is that a keystone of therapy in osteoporosis is a substantial protein diet. In severely protein-depleted persons the synthesis of osteoid tissue is compromised and, consequently, calcification is decreased, since there is less space for calcium deposition. This leads to an extra-osseous surplus of calcium in the body (41). Thus a patient in a state of inanition is a choice candidate for the inception of osteoporosis.

The protein may not be available because of a) inadequate intake, as in malnutrition (68), b) malabsorption or improper assimilation, as in sprue or chronic hepatic disease (69, 70), c) excessive loss, as in nephrosis (71) or extensive burns (72), or d) because it is diverted towards caloric requirements, as in hyperthyroidism, uncontrolled diabetes, or surfeit of adrenocortical hormones from endogenous or exogenous sources. Although thyroxine, insulin and corticoids are not directly related to dietary considerations, they will be discussed briefly here because of the bearing they have on protein metabolism.

Thyroxine accelerates the rate of activity of all biologic systems. Thus in hyperthyroidism there is a greater quantitative need for all materials involved in these processes, increased amounts of protein becoming consumed thereby (3, 73–76).

Absence of insulin entails a relative nitrogen starvation due to increased gluconeogenesis with diversion of amino-acids from protein synthesis. Moehlig (77, 78) reported diabetic type glucose tolerance curves in many instances of senile osteoporosis. Hernberg (79) found osteoporosis to be a presenile change occurring fairly regularly in adult diabetics. It has not been corroborated that osteoporosis may be prevented by keeping the blood sugar concentration at a low level with large doses of insulin.

Cortisone and similar substances are antianabolic; they also stimulate the rate of glucose formation from noncarbohydrate precursors by gluconeogenesis. They may likewise accentuate calcium loss by a direct effect on calcium excretion. The prolonged administration of such steroids is not without peril. Indeed, there have been several reports of osteoporosis and vertebral collapse following the use of adrenocorticoids (80–91). The issue is clouded, in that most of the cases studied presented situations predisposing to bone disease. Hjorth and Dragsted (92) are of the opinion that osteoporosis is not a contraindication for a brief period of treatment with ACTH. Luder (93) considers osteoporosis to be a development of relative benignity in conditions in which prolonged courses of cortisone are indicated. Presumably, this complication could be counteracted by the simultaneous use of testosterone (94, 95). Along these same lines, it is noteworthy that ACTH and cortisone are allegedly useful in the treatment of reflex sympathetic dystrophy (96). Akin to this condition is the post-traumatic painful osteoporosis described by Sudeck (97), an obscure condition about which knowl-

edge is decidedly incomplete (98–105). Adrenocortical steroids should be used with much caution in Sudeck's atrophy, and only as an adjunct to older standbys such as physiotherapy, and medical or surgical sympathectomy (106).

The endogenous form of hypercorticalism, or Cushing's disease, is attended by one of the most severe forms of osteoporosis. Management is with gonadal hormones (see the following section).

The imbibition of large volumes of water is indicated principally in immobilization osteoporosis, in order to dilute the urine and obviate the tendency to formation of calculi. In acute states of the disease, ingestion of excessive calcium or vitamin D is contraindicated, since it may aggravate hypercalciuria. In later phases of management, on the other hand, moderate quantities of these substances ensure proper calcification of matrix. The beneficial role of minerals obtains from an inhibition of bone resorption, rather than a stimulation of osteoblastic activity. Because the net mineral loss in osteoporosis may be considerable, replacement requires a very long time. "On an ideal high protein, calcium, phosphorus, vitamin and gonadal intake, the maximum retention will not exceed 2 grams of calcium per day. Therefore to replace 2 or more pounds will require 1000 days" (40). Recovery from advanced bone atrophy is very slow if, indeed, it is ever completed.

With reference to vitamins other than calciferol, the vitamin B complex may be included in the diet, since components of this complex aid in the utilization of protein. Hallahan (107) reported that osteoporotic patients treated with vitamin B_{12} obtained subjective relief by the first week of therapy and became entirely asymptomatic by the third week. The reason for this ostensible effectiveness of vitamin B_{12} is an enigma. Vitamin C is a required component in the therapeutic regimen. Scorbutic osteoporosis is due to a generalized paucity of cement substances, the counterpart of which in the bones is poor matrix formation (76).

Gonadal hormones

It has been contended that a moderate degree of osteoporosis is an almost "physiologic" accompaniment of old age in either sex (5, 7), senescence being heralded ordinarily by a state of "catabolic ascendancy" reflected in atrophic and degenerative changes throughout the body, including the skeleton (108, 109). Indeed, the postmenopausal type is the most prevalent form of osteoporosis, aside from being the commonest of systemic osteopathies (5). More than half of all women more than 50 years of age show x-ray manifestations of diminished bone mass. The real percentage is higher, undoubtedly, considering lesions unrevealed radiologically. Only about one-tenth of the group, however, present themselves with symptoms.

The classic studies of Albright, Reifenstein and their associates on what they designated "postmenopausal osteoporosis" brought to the fore much of the present interest in osteoporosis in general (22, 23, 5, 110, 111). These workers pioneered in the use of gonadal hormones for the treatment of this condition, on the basis of a surmise that it is the diminution of these agents in old age which

gives rise to the osteoporosis. It is true, nonetheless, that the clinical picture which ensues is a product also of the status of the patient at the time gonadal insufficiency becomes manifest (*e.g.*, diet and physical activity), as well as the rate of development of the latter. Thus, in a series of 289 osteoporotic subjects between the ages of 40 and 60 studied by Anderson, 234 were women (112). The explanation ventured is that, since the onset of the menopause is far more precipitous than that of the "Leydig-pause," the brunt of cessation of gonadal function is experienced sooner in the menopause (110). Hence the lower incidence of osteoporosis in elderly males as compared to members of the opposite sex in the same age group (113). This becomes more apparent in studying men who have undergone castration and in whom osteoporosis is more frequent and severe.

Postmenopausal osteoporosis refers to the condition in females less than 65 years of age. Senile osteoporosis of women refers to the disorder when it occurs after 65 years of age. This chronologic differentiation is altogether arbitrary and bears no strict relation to the clinical situation. There appears to be no symmetry between the severity of menopausal symptoms and the onset of osteoporosis. Albright and Reifenstein (5) are inclined to the view that an artificial menopause is associated with more marked osseous atrophy than is a functional menopause. This impression has been disputed recently by Donaldson and Nassim (114). At all events, it appears that the degree of osteoporosis also increases with the duration of hypoestrinism.

The value of the sex hormones in osteoporosis lies in their diverse effects on bone metabolism. These hormones have a general protein anabolic action, and stimulate the growth of all tissues, including osteoid. The androgenic effect on nitrogen retention is considerably more sustained than that of estrogens. Both hormones decrease urinary and fecal calcium and phosphorus excretion in all forms of osteoporosis except the idiopathic type (3). The estrogenic effect on calcium retention transcends that of androgens. The level of serum inorganic phosphorus which tends to be high in postmenopausal cases, falls during administration of sex hormone. The alkaline phosphatase level is ordinarily not influenced by gonadal hormones, an exception being the rise observed during the treatment of Cushing's syndrome with androgens. Estrogens are believed to have a specific energizing effect on osteoblastic activity. Androgens also presumably stimulate the patient's psyche, resulting in a feeling of increased well-being.

Hormonal therapy gives osteoporotic patients a new lease on life. The most striking effect is mitigation of pain, usually within the first two weeks of treatment—a period much too short to allow for any possible change in the bone matrix. No adequate explanation for this dramatic cessation of pain has been proffered. The patients lose their lassitude, become animated, and regain their appetite. Objective improvement is slow to appear, and consists mainly of a diminution of articular limitation, strengthening of previously shrunken muscles, a gain in weight, and improved healing of fractures. Even in advanced cases in which the osseous lesions cannot be restored to normal, hormonal therapy causes osteoporosis to regress or become stabilized (115, 116). Despite this clinical amelioration, radiographic verification thereof is not discernible. Schoene's paper

(24) is one of the most enthusiastic of the sundry articles reporting the efficacy of anabolic steroids in osteoporosis.

It is to be expected that long-term administration of such potent agents might lead to adverse side-effects. Estrogens induce "rejuvenating" changes in the elderly female, such as mammary and pelvic congestion, and endometrial hyperplasia with bleeding. Although there is no convincing proof that sex hormones may be tumorigenic in the human, their possible role as co-carcinogens is still subject to considerable debate. Androgens in large dosage give rise to virilizing changes in women, such as hirsutism, deepening of the voice, acne, and clitoral turgescence and hypertrophy. These can be the source of much social mortification. Reports are accumulating to the effect that combinations of estrogens and androgens are superior therapeutically to either alone (110, 117–119). A synergistic result in beneficial actions, such as calcium retention, accrues from their joint administration, and precludes the development of harmful side-effects, such as masculinization and metropathia. However, in certain instances in which the sex steroids produce harmful results not neutralized by their co-administration, other measures may be necessary. Thus, if edema should develop because of excessive retention of extracellular fluid, the sodium intake should be reduced (117, 120), and this step followed by appropriate diuretics if necessary. The entire subject has been discussed elsewhere (121). There is an ever-growing trend nowadays to employ the newer weakly-virilizing androgens in gynecologic endocrinology. Methylandrostenediol is such a preparation, and favorable results from its use in osteoporosis have already been reported (122, 123). The outcome of further experiences with its application in this disorder is awaited with interest.

It should be emphasized that estrogens must always be administered intermittently. Androgens may be given either intermittently for the same length of time as the estrogenic agent or continuously. It is advisable to warn the patient that, under a regimen of interrupted estrogenic therapy, some vaginal bleeding is to be expected during the interval when the drug is omitted temporarily. Bleeding at any other time should be reported to the physician and be the signal for instigating a meticulous search for a possible pathologic condition in the genital tract. With the androgen program, since cutaneous oiliness is one of the initial signs of impending virilizing changes, the texture of the skin is usually a good guide to dosage (124).

Because osteoporosis appears to be a concomitant of advancing years, it has been advocated that all women should receive gonadal hormones prophylactically in order to avoid its development. There has not been any well-planned study reported as yet, but a number of critical physicians have hazarded the impression that such a preventive program has yielded over-all favorable results on a small scale.

The osteoporosis of Cushing's syndrome is ameliorated by testosterone because of the counterbalancing effect of this steroid on the excessive production of anti-anabolic substances in this condition (5, 125, 126). Dunn (127), and Rakoff, Cantarow and Paschkis (128) reported beneficial results clinically in Cushing's syndrome treated with estrogens, an effect which Albright (111) ascribes to

restitution of the calcium balance. It is interesting that in panhypopituitarism, although both adrenocortical and gonadal hormones are markedly reduced, balance is maintained so that osteoporosis does not ensue (110).

Benefit is obtained in acromegalic osteoporosis by the use of gonadal hormones (129–131). The pathogenesis of the osteoporosis here is an intricate one, being contributed to by the excess of growth hormone, the secondary hypogonadism (5), and the hyperthyroidism (124) and diabetes (124, 132) which may be associated with acromegaly.

A positive calcium balance and clinical improvement can also be attained with both sex hormones in the hereditary form of osteoporosis known as fragilitas ossium (133). In this disease, sparseness of bone matrix is traced to an intrinsic defect in the activity of the osteoblasts which, however, are present in adequate numbers (134). As the name connotes, the bones are frail and brittle, and vulnerable to numerous fractures following minor traumata. Other tissues of mesenchymal origin in the body are also deranged and thin. There is a tendency toward improvement when adult life is reached. Gonadal hormones, by stimulating osteoblastic function, aid in attempting to restore a normal pattern of osteogenesis.

Albumin

A singular group of osteoporotic patients are those in whom, after a process of etiologic elimination, the condition is found to be primary. In these cases, none of the factors listed in Table 2 can be incriminated. The patients are usually young adults with normal gonadal function (134). In men, the condition may follow a seemingly insignificant accident, and be without antecedent symptoms. Women may succumb to it after a normal pregnancy (135–139). Although it is tempting to attribute the skeletal rarefaction in parturient osteoporotic subjects to the increased calcium requirements during pregnancy, there is usually nothing in their histories suggestive of inadequate calcium or calciferol intake (137). Recently, Bayliss and his associates (138) postulated that the association between pregnancy and osteoporosis may be more than fortuitous, and invoked as a possible explanation the high level of circulating plasma corticosteroids during parturition. Conventional therapeutic measures have proved valueless in rectifying idiopathic osteoporosis. The sole effective agent is intravenously administered serum albumin (140).

Albright and his associates adduced from their metabolic studies on the fate of intravenous proteins in idiopathic osteoporosis that albumin may possibly be a transport form of bone matrix precursor (141–145). In patients studied during a constant metabolic regimen, intravenous albumin produced a rise in the level of serum calcium, a retention of salt and water, and a decreased urinary excretion of potassium, phosphorus and calcium. Thus the effect of intravenous albumin is analogous in some respects to the action of estrogen. Circumstantial evidence of the role of serum albumin as an important building block of matrix is afforded by Emerson and Beckman's observation (71) of severe osteoporosis in nephrosis. Moreover, Albright (110) studied 2 patients with idiopathic osteo-

porosis in whom nephrosis was aggravated by renewed pregnancy, a state in which there is hypoalbuminemia, aside from increased influence of corticoid.

A paradoxical observation is a fall in the serum alkaline phosphatase level, instead of the anticipated rise due to increased osteogenesis. Another discrepancy is illustrated by the observation that in one of their patients in whom intravenous globin was given, Albright *et al.* (145) observed a decrease in urinary calcium excretion that was of the same order of magnitude as would be obtained with albumin. This raises some doubt as to the specificity of albumin as the sole precursor of osteoid.

These problems notwithstanding, the use of albumin in osteoporosis seems promising, and opens several new vistas in research. Thus, as Reifenstein (3) has suggested, "The possibility of giving a course of albumin therapy at the time when a patient with severe postmenopausal osteoporosis is started on steroid medication deserves investigation. Such a procedure might accelerate the rate of increase in bone formation, and might bring the clinical manifestations under control more rapidly than the steroid therapy alone."

Strontium

This cation is currently the subject of much interest. It is not an abundant element in nature, its concentration in ingested foodstuffs is nil for all practical purposes, it is present only in trace amounts in the human body (146), and it plays little if any role in normal animal physiology.

Lehnerdt (147, 148) was one of the earliest investigators to study the action of strontium on bone. He concluded that the effect was twofold—an augmented production of osteoid, and increased mineralization thereof. The work of Shipley and his associates (149) refuted this contention of increased osteoid production. Alwens (150) envisioned the possibility of employing strontium as a means of accelerating remineralization of the skeleton in nutritional osteoporosis. Shorr and Carter (151–155) are principally responsible for evaluating strontium in postmenopausal osteoporosis.

Strontium functions apparently as an additive mineralizing factor by enhancing calcium absorption and storage. It does this when the phosphorus intake is adequate, since it is utilized as strontium phosphate. If the phosphorus level is low, strontium will compete with calcium and protein for the available phosphate. In fact, when vitamin D is eliminated from the diet and patients are maintained on a low intake of calcium and phosphorus, strontium can be used to induce an osteomalacic state. It becomes evident, then, that the use of strontium in the therapy of osteoporosis must be governed delicately by an optimum intake of protein, calcium and phosphorus. Although strontium may be administered as strontium phosphate, the lactate appears to be better absorbed and tolerated (151). The element is innocuous, even when administered in rather large amounts and over long intervals (156, 157).

Exactly how strontium causes increased calcium storage is unknown. Radioactive tracer studies (158–161) have indicated that the distribution of strontium is virtually limited to bone, and that its movement in and out of the skeleton is

similar to that of calcium (162, 163). Strontium lactate is absorbed to a greater degree than calcium lactate when administered in equivalent amounts (151). Shorr and Carter (152) reported that the sum of strontium and calcium retained with a constant phosphorus intake in postmenopausal osteoporosis was greater than the maximum retention of calcium when it was given alone. Androgens, estrogens, and calciferol increased the storage of both strontium and calcium. However, since androgens are protein anabolic agents, they may prevent strontium absorption if the phosphorus intake is low, because the phosphate present becomes unavailable by reason of its being combined in nitrogen storage.

Experience in another clinic with the application of strontium lactate in osteoporosis is forthcoming (164).

Anti-algesic and other supportive measures

Testosterone is probably the most effective agent for the alleviation of pain in osteoporosis. It is questionable whether intraganglionic injections of alcohol and nerve section (165) are ever warranted, except perhaps in extreme cases. Analgesics, such as the salicylates, are useful in curtailing discomfort. One is not too impressed by the relief imparted in 45 per cent of senile osteoporotic patients by phenylbutazone given in conjunction with sex steroids (166). Since analgesia incident to androgenic therapy alone is usually greater, one can argue that inclusion of phenylbutazone in the program may actually vitiate the effects of hormonal treatment. Besides, the use of this drug is fraught with harmful side-effects (166–167). Sedatives can also be incorporated in the therapeutic regimen. They should be administered with discrimination in the geriatric patient (168, 169), because of the presence of arteriosclerotic changes, increased capillary permeability, and hemoconcentration. Barbiturates often have a prolonged effect because of lessened permeability of the kidney. Should the use of narcotics be contemplated in the aged, one must be alert to the likelihood of dosage-response inconsistencies, and dependency. The possible hazard of the frequent use of radiotherapy to assuage pain (129) or for other purposes, has been mentioned.

The control of local and radiating pain is promoted by physiotherapy and orthopedic rehabilitation through calisthenic and passive exercises. Spinal supports should be permitted only for short periods, and only as a last resort in patients with pronounced deformities not corrected by other means (170). Massage and moderate local heat are of help in relaxing aching muscle spasm. Some physicians (170) state that shortwave diathermy should not be used, since it is presumed to cause increased vascularity, and there are still those who maintain that hyperemia aggravates osteoporosis. This viewpoint has been challenged by other investigators (171).

Aside from a balanced diet with supplementary food concentrates, blood transfusions are very useful in raising the general body resistance and providing readily utilizable protein. In aged patients, hypostatic pneumonia and hypervolemia should be guarded against in the administration of infusions.

An important feature of management is the avoidance of sleeplessness, tension, anxiety, exhaustion and infections, since osteoporosis may be aggravated by

these disturbances, presumably through the intermediary of the stress syndrome (172–174).

SUMMARY

The pathogenesis of osteoporosis stems from impoverished bone matrix. What distinguishes the limits of variation in composition of normal osseous tissue from deviations leading to osteoporosis is the maintenance of optimum conditions of all the metabolic and mechanical influences concerned with osteogenesis.

In its fully developed form, osteoporosis offers little difficulty in the way of diagnosis. It is the incipient lesser grades which are likely to be overlooked, particularly when attention is distracted by the presence of other coincident disorders. The detection of osteoporosis in its nascent and most remediable stage depends almost exclusively on an awareness of the situations in which it may occur. Early diagnosis, then, is anticipatory for the most part.

All possible factors contributing to the clinical picture of osteoporosis must be ferreted out before the condition may be ascribed to a single disease entity. Moreover, in advanced cases one often faces indeterminate types so irregular that they defy classification. Accordingly, an exact estimation of the nature of the specific disorders accounting for osteoporosis in a given patient can only be achieved when a chain of evidence, both positive and negative, points unequivocably toward such a conclusion.

Since in most cases of osteoporosis multiple factors are operative, it is generally difficult to evaluate the precise part played by each. Treatment needs to be formulated according to the circumstances of the individual case. In a particular instance, therefore, more than one of the following measures will be instituted: mobilization and exercise, high-protein diet, fluids, vitamins, minerals, and gonadal hormones. In addition, albumin and strontium have come under scrutiny recently as therapeutic adjuncts.

Prolonged immobilization and recumbency result in deprivation of the stresses necessary for the stimulation of osteoblastic function, and in profound metabolic disturbances. Maximal mobility, weight-bearing, and exercise must be applied, in conjunction with restrained calcitherapy, in order to offset such serious consequences as multiple fractures and nephrolithiasis.

Gonadal hormones act by virtue of their general tissue anabolizing effect and their influence on calcium and phosphorus metabolism. Their beneficial action in different types of osteoporosis is manifested by abolishment of pain, pronounced subjective improvement, and reinstatement of tissue mass and strength.

Dietetic considerations involve replenishment of attenuated protein stores to provide osteoblasts with material for matrix production. The incorporation of minerals and vitamin D in the diet should be executed with reservation. Fluids and other vitamins enhance the therapeutic regimen.

Serum albumin (intravenously) is the single substance effective in idiopathic osteoporosis. It is presumed to be the possible immediate precursor of bone matrix. Its effect in other types of osteoporosis awaits trial, and its precise relationship to osteoid remains to be clarified.

Much more investigation is needed with reference to the metabolism of strontium. Its seeming mineralizing potentiation, delicately influenced by phosphorus levels, deserves particular attention in view of the interesting possibilities it has to offer in the therapy of osteoporosis and other disorders of bone.

A keen awareness of possible complications is required in the administration of such agents as sedatives, narcotics, local heat, and transfusions in the geriatric patient with osteoporosis.

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SERUM CHOLESTEROL LEVELS RESULTING FROM VARIOUS EGG DIETS—EXPERIMENTAL STUDIES WITH CLINICAL IMPLICATIONS*

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Reference to hypercholesterolemia induced by feeding eggs is being transmitted from one text to another, but the number of studies on which such references are based is small.

Comparison of available data is difficult. Some experiments lasted only four days (1), but others lasted forty-eight days (2), six to ten weeks (3), or six months (4). Dogs (3), monkeys (1), rats (4), guinea-pigs (5), golden hamsters (5), rabbits (5, 6) and human beings (2, 3) were given some of the following daily: 2 to 5 whole eggs (1), 2 to 5 egg yolks (1), half an egg yolk plus 0.5 Gm. of cholesterol (5, 6), 100 Gm. of egg powder (3), egg powder *ad libitum* (4), 100 to 150 Gm. of egg powder in 400 ml. of milk (2), or baked cakes containing 4 parts of egg powder, 1 part of flour, and yeast, water and salt (5). Moreover, the composition of the egg powder was not always known, and varied when it was known.

There are many discrepancies in the experimental results, but the authors all maintain that the hypercholesterolemic effect of egg consumption is due to the cholesterol content of the eggs. Therefore, investigation of the effects of various egg preparations and combinations on the blood cholesterol level of rabbits seemed desirable.

MATERIALS AND METHODS

Ninety male rabbits of uniform breed, weighing 3½ pounds each, were given a basic diet of Purina rabbit chow. They were divided into series of 6 animals each and observed for four weeks. The first blood sample was drawn after one week of basic diet; 3 further samples were obtained after seven, fourteen, and twenty-one days of egg diet. Blood was assayed for total, free, and esterified cholesterol (7).

The rabbits in series I received 1 raw egg yolk, daily; in series II, 1 raw whole egg; in series III, 1 soft boiled egg (two minutes at 100°C.); in series IV, 1 egg scrambled with 1 Gm. of Crisco (two minutes at 120°C.); in series V, 1 poached egg (two minutes at 100° C.); in series VI, 1 egg baked in a cake with 35 Gm. of ground rabbit chow (thirty minutes at 450° C.); in series VII, 1 egg which had been baked in the shell (thirty minutes at 450° C.); in series VIII, 1 hard boiled egg (eight minutes at 100° C.); and in series IX, 1 egg fried in 1 Gm. of butter (one and a half minutes at 320°C.). Each rabbit consumed 21 eggs in as many days.

Rabbits in series X and XI were observed for forty-six days. Blood cholesterol concentration was determined weekly. The rabbits in series X received 1 whole raw egg daily (a total of 42 eggs); and in series XI, 1 raw whole egg once a week (a total of 7 eggs in forty-two days).

On analysis of the results with these egg diets, extension of the study was found neces-

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sary. Four additional series of rabbits were fed daily 180 mg. of powdered cholesterol (C. P., Pfanstiehl) for twenty-one days. The animals in series XII received untreated powder (as raw egg) sprinkled on the chow; in series XIII, cholesterol heated for two minutes to 100° C. (as soft-boiled egg); in series XIV, cholesterol heated for thirty minutes at 450° C. with rabbit chow (as baked egg); and in series XV, 180 mg. of cholesterol fried with 1 Gm. of butter (as fried egg).

RESULTS

The results of egg feeding are presented in Figures 1 and 2. Absolute blood cholesterol values are plotted in the first graph. The blood cholesterol concentration varied from animal to animal and from series to series. Therefore, pre-experimental levels were converted to the same height and all following values expressed in multiples of pre-experimental levels. Corrected averages are shown in Figure 2. The correction resulted in reversed sequence of series VII and VIII in both graphs.

Using the number 100 for the average initial blood cholesterol level, the values after seven, fourteen, and twenty-one days were: for series I, 160, 162, 268; for series II, 130, 310, 330; for series III, 140, 204, 404; for series IV, 216, 354, 518; for series V, 220, 422, 608; for series VI, 124, 524, 632; for series VII, 188, 434, 716; for series VIII, 226, 852, 1,022; and for series IX, 510, 696, and 1,404.

After one week of a fried-egg diet the blood cholesterol level was higher than after three weeks of a diet of raw yolk, whole egg, or soft-boiled egg, and as high

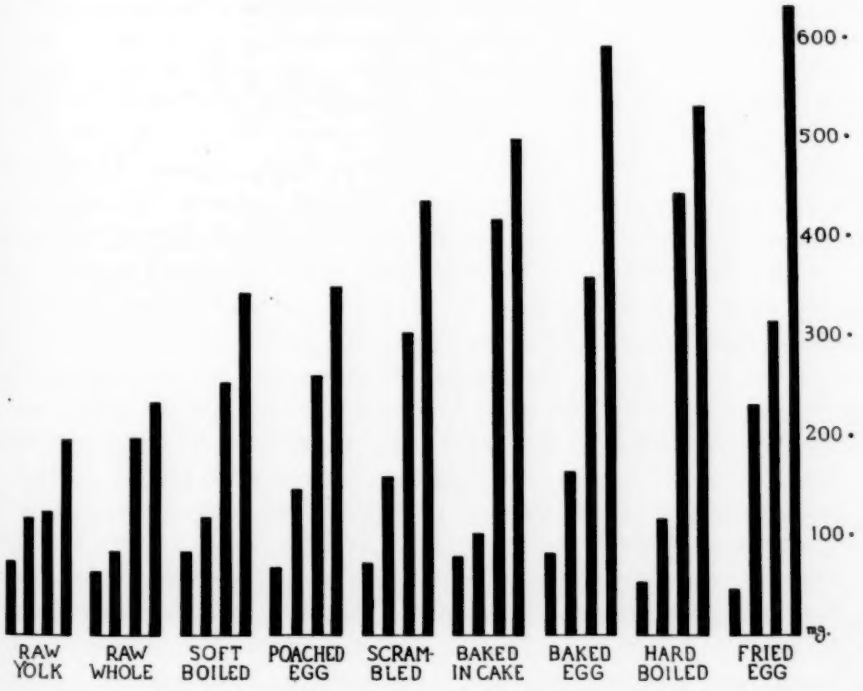

FIG. 1. Average blood cholesterol levels (mg./100 ml.) in the rabbit, before and after various egg diets. First column, pre-experimental; second column, after 7 days; third column, after 14 days; and fourth column, after 21 days of egg diet.

FIG. 2. Increase in average values for blood cholesterol in the rabbit (expressed in multiples of pre-experimental level) during ingestion of various egg diets. First column, pre-experimental; second column, after 7 days; third column, after 14 days; and fourth column, after 21 days of egg diet.

as after three weeks of a diet of scrambled eggs. The changes in the blood cholesterol levels during the three-week period were of interest. In series I through V there was a fairly even increase from week to week. In series VI through VIII the rise was slight after seven days, marked after fourteen days, and not quite so great after twenty-one days of diet. In series IX the cholesterolemic effect was severe in the first and third weeks but slight after the second week of the diet.

Though there was considerable variation within each series, comparison of minimum, average, and maximum cholesterol values yielded parallel graphs. Differences in the effects of various egg preparations were marked, whether one compared absolute or relative values. Curves for free and esterified cholesterol resembled closely those for total cholesterol and need not be reported separately.

Rabbits of series XI fed a raw whole egg once a week for six weeks had, on the twenty-third and on the forty-sixth day of observation, almost exactly half the concentration of blood cholesterol level as did rabbits of series X which consumed seven times the number of eggs. The respective levels were 3.6 and 3.25 times the pre-experimental value in series X, and 1.56 and 1.53 times in series XI.

In the rabbits of series XII through XIV, fed 180 mg. of cholesterol a day for twenty-one days, average initial and final absolute total cholesterol values were 60 and 145, 75 and 212, 62 and 210, and 65 and 240 mg. per 100 ml. of blood respectively. In multiples of 100 (for pre-experimental levels) the final values were 240, 280, 310, and 369 for the four series.

DISCUSSION

The experiment had several limitations. Though eggs were secured from a single supplier they differed in total weight, thickness of shell, volume and weight of egg white and yolk, the amount of cholesterol, and probably the amount of all the other constituents. The rabbits did not eat exactly the same quantities of egg or chow, nor did they eat at the same pace. All animals ate the egg dishes mixed with rabbit chow readily. They were especially eager to eat fried and scrambled eggs.

Varied response to egg diets cannot be explained by interaction of biotin and avidin. Although it is uncertain whether biotin enhances hypercholesterolemia, it is known to promote the deposit of cholesterol in organs of animals (8–11). Avidin, present in yolk, counteracts biotin (12, 13). Since avidin is destroyed by heat, one would expect differences in response to raw and heated egg. However, variations in the effect of eggs treated for different lengths of time and to different degrees could not be explained by inactivation of avidin.

The responses to cold cholesterol powder and to cholesterol heated for varying times and to varying degrees were not as marked as the responses to egg preparations, but were still distinct. In an attempt to explain the results, the cholesterol powder was subjected to analysis. Comparison of the cholesterol used (C.P., Pfanstiehl) with a standard prepared from purified cholesterol yielded 85 per cent color strength in the Burchard-Liebermann reaction. When the powder was heated for two minutes at 100°C. the yield was 93 per cent. Prolongation of time beyond two minutes, or increase of temperature above 100°C. did not further intensify the color reaction. The product melted at 300°C.

The stronger cholesterolemic effect of heated cholesterol can be explained. Although all rabbits ate 180 mg. of cholesterol powder daily, those in series X received 153 mg. of Burchard-Liebermann-positive material, those in series XI and XII received 167.4 mg. of reacting material, and those in series XIII received heated powder plus 1 Gm. of heated butter with a total of 168.94 mg. of Burchard-Liebermann-positive material per day.

Animal brain is the common source of commercial manufacture of cholesterol. It may be assumed that, on heating, some constituents of cholesterol powder change to cholesterol or to related compounds which produce a color reaction with acetic anhydride-sulphuric acid reagent. Analysis of all commercially available cholesterol preparations seems warranted, since it could explain discrepancies in experimental results of various investigators.

The effect of heat on the egg was also studied. Because of significant variations, batches of 10 eggs were analyzed or pooled and aliquots were tested. The average weight of the shelled eggs was 50 Gm. (20 Gm. contributed by egg white, and 21 Gm. by cholesterol-bearing yolk). The shell weighed 3 Gm. on the average. The level of Burchard-Liebermann-positive material in shelled raw eggs averaged 433 mg. per 100 Gm. The average for soft boiled eggs (two minutes at 100°C.) was 524 mg.; for hard boiled eggs (eight minutes at 100°C.), 645 mg.; and for eggs baked in the shell (thirty minutes at 450°C.), 660 mg. per 100 Gm. The average for eggs fried with 1 Gm. of Crisco per egg (one and a half minutes

at 320°C.) was 520 mg.; for eggs fried with 1 Gm. of butter per egg (one and a half minutes at 320°C.) it was 660 mg.; and for eggs scrambled with 1 Gm. of Crisco per egg (two minutes at 120°C.), it was 500 mg. per 100 Gm.

The difference between the cholesterolemic effect of raw yolk and that of raw whole-egg feeding (series I and II) was slight. Soft boiled eggs (series III) were less effective than poached eggs (series IV), though both types were heated for two minutes at 100°C. Apparently the shell shielded the yolk from the heat part of the time. These results established the importance of the length of time during which the egg had been heated. This became even more evident after a diet of hard boiled eggs (series VIII), which caused severe hypercholesterolemia.

Scrambled eggs (series V) were heated with Crisco for two minutes at 120°C., out of the shell. Therefore, it was not surprising that the blood cholesterol level of rabbits in series V rose higher than in rabbits receiving a soft boiled or poached egg diet. Differences between the effect of eggs baked in the shell (series VI) and that of eggs baked with chow (series VII) were slight. It should be noted that 100 Gm. of raw Purina rabbit chow yielded 154 mg., and 100 Gm. of chow heated for thirty minutes at 450°C. yielded 170 mg. of Burchard-Liebermann-positive material. If the reaction in chow is caused by sitosterols, an explanation for the lesser hypercholesterolemic effect of baked egg-chow cakes compared to baked eggs would be provided. Protection of the egg shell against the heat (450°C. applied for thirty minutes) would be negligible and would hardly affect the results.

A maximal increase of blood cholesterol concentration was obtained in rabbits fed eggs fried in butter (series IX). The period of heating was short and the temperature was lower than in baking. On heating the butter for one and a half minutes at 320°C., the yield of Burchard-Liebermann-positive material was 154 mg. per 100 Gm. Thus, the amount of presumably hypercholesterogenic substance fed to these rabbits was considerably higher than that consumed by the other animals.

Okey (14), in comparing the available data on cholesterol in egg, egg yolk, and butter, converted the values based on dry weight to those based on fresh weight. Cholesterol was calculated as 2,000 mg. per 100 Gm. for fresh egg yolk, 2,810 mg. for Chinese dried, 3,900 mg. for dried, 1,750 mg. for vacuum dried, 1,365 mg. for frozen, and 1,272 mg. per 100 Gm. for commercial frozen egg yolk. Cholesterol was assayed as 468 mg. per 100 Gm. in fresh whole egg, 562 mg. in commercial frozen, 600 mg. in frozen, and 2,770 mg. per 100 Gm. in commercial dried whole egg. The cholesterol content of butter has been reported as 71 mg., 185 mg. and 280 mg. per 100 Gm. respectively, by 3 different authors.

Due to variation of source, the exact composition of these products cannot be established. Normal egg yolk contains roughly 62 per cent triglyceride, 33 per cent phospholipids, and 5 per cent cholesterol. (Our eggs contained an average of 4.33 per cent cholesterol.) Fatty acids contain about 50 per cent oleic acid, 27 per cent palmitic acid, 11 per cent linoleic acid, 6 per cent stearic acid, and 6 per cent other acids. Some of these substances affect the absorption of cholesterol; thus, following chemical changes caused by heating, absorption may be altered.

It is impossible to apply the results of animal experiments to man. Rabbits (series I through X), weighing 3½ pounds each, received daily from 91 to 165 mg. of cholesterol (more correctly of Burchard-Liebermann-positive material) in the form of egg. A man weighing 50 times as much as the rabbit, *i.e.* 175 pounds, would have to ingest 4.5 to 8.25 Gm. of cholesterol daily. Rabbits of series XI ate 91 mg. once a week. Consumption of 4.5 Gm. of cholesterol per week would not be unusually high for an adult man. However, a man would not consume all cholesterol in the form of 50 raw eggs on one day and then eat a cholesterol-free diet for six days. The consumption of cholesterol by man may be considerably higher than is generally believed. Calculations of diets are based on analysis of raw materials. We found that the amount of Burchard-Liebermann-positive (and presumably hypercholesterolemia-promoting) material introduced into the digestive tract in the form of an egg fried in butter exceeds by 83 per cent the amount introduced by a raw egg, and exceeds by 50 per cent the amount ingested in a soft boiled egg. In rabbits, hypercholesterolemia after twenty-one days of a fried egg diet was 4.25 times higher than after a raw egg diet, and 3.5 times higher than after a soft boiled egg diet.

Investigation of the effect of heating on the cholesterol content of various foodstuffs seems desirable. We may have to revise our diets for persons with a tendency toward hypercholesterolemia by paying as much attention to the preparation of the food as to the components of the diets.

SUMMARY

Groups of rabbits were fed various egg dishes daily for three weeks.

Marked changes in blood cholesterol levels were noted as a result of the egg diets. Ingestion of raw eggs caused a three-fold increase, and a diet of eggs fried in butter caused a fourteen-fold increase; other egg preparations induced increases that ranged between these two extremes.

Feeding of cholesterol powder treated in the same manner as eggs had varied effects on the blood cholesterol level. Experiments with cold and heated cholesterol powder, and determination of cholesterol in eggs heated for varying lengths of time to varying temperatures, in butter, in Crisco and in chow, aided in interpretation of the findings.

Implications of the experimental results as applied to man are discussed.

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IRON THERAPY FOR AGED PATIENTS

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Side-effects of iron therapy are common among aged patients, possibly because aging causes atrophic changes in the mucous membranes and secretory cells of the gastro-intestinal tract which make these organs particularly susceptible to injurious stress (1). Although irritation by iron salts is seldom severe, it can be annoying. Elderly patients suffering from even mild abdominal cramps or constipation will usually refuse further medication.

This report concerns the evaluation of a new iron preparation for efficacy in the treatment of anemia, and the incidence and severity of side-effects in geriatric patients. This preparation provides dispersion and sustained release of small amounts of ferrous salts throughout the upper and middle small intestine. The iron in each capsule dose is in the form of many tiny, coated pellets. The coating on the pellets keeps the iron in the active ferrous form and permits the slow release of these ferrous salts throughout the portions of the intestine from which satisfactory absorption may be expected. Only a small amount of iron is released at any one site. This, in theory, should reduce the chances of irritation of the mucous membranes and secretory cells of the intestine.

PATIENTS AND METHODS

Ten of my most aged iron-deficient patients were treated with the sustained-release capsules of iron. The average age of these patients was 81.4 years; the youngest, a man, was 64; the others were women between the ages of 72 and 97. In all there was a clear history of inadequate dietary intake of iron. They lived at home alone or with their families, and their diets and eating habits were not properly supervised. All were known to have constipation or abdominal cramps as side-effects of conventional iron therapy.

The hemoglobin levels were below the normal range determined by Hobson and Blackburn (2) for aged patients living under similar home conditions.

Each patient was given 1 sustained-release capsule daily, containing 150 mg. of exsiccated ferrous sulfate.[1] The women received medication for forty-nine days, and the man for sixty days.

RESULTS AND DISCUSSION

In the 10 patients of the study, the control level of hemoglobin ranged from 7.5 to 11.5 Gm. per 100 ml. (average, 9.2 Gm.). During sustained-release iron therapy, the hemoglobin level in 8 of the 10 patients rose to within the normal range established by Hobson and Blackburn. The increases varied from 0.5 to 6.0 Gm. per 100 ml. (average, 2.6 Gm.), the final range being 10.0 to 14.5 Gm. per 100 ml. (average, 11.8 Gm.). In 1 of the remaining 2 subjects, the hemoglobin level rose from 8.5 to 9.0 Gm. per 100 ml. but did not reach the normal value;

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[1] Supplied for investigational use by Smith, Kline & French Laboratories, Philadelphia, Pennsylvania.

in the other, the level did not change. It is beyond the scope of this report to consider the many possible reasons why these 2 patients had suboptimal responses.

There were no side-effects from sustained-release iron therapy, although all the patients had been constipated or had abdominal cramps during treatment with conventional iron preparations. Ordinarily, as Stieglitz points out (3), when iron is given to aged patients, the physician must see that they maintain adequate bowel movements, even to the point of prescribing the concomitant use of cathartics. In the present study, an example of the effects was the case of a woman who had required a daily cathartic for as long as she received conventional iron preparations (even when given in reduced dosages); during sustained-release iron therapy, she had normal bowel movements without catharsis. In this patient, the absence of constipation was especially gratifying.

An incidental observation was that the patients preferred the convenience of the single daily dose of sustained-release iron, compared to the thrice-daily doses of ordinary iron medications.

SUMMARY AND CONCLUSIONS

Ten aged patients with iron-deficiency anemia (average hemoglobin level, 9.2 Gm. per 100 ml.) were given 1 sustained-release capsule daily, containing 150 mg. of exsiccated ferrous sulfate. Within two months, the hemoglobin levels had returned to normal in 8 patients—average, 11.8 Gm. per 100 ml. In 1 other patient there was an increase, but not to the normal level; and in 1 patient there was no change.

All patients had suffered from side-effects (constipation or abdominal cramps) during conventional iron therapy, but there were no side-effects during treatment with iron in the sustained-release form.

The efficacy, the lack of side-effects, and the convenience of the single daily dose of sustained-release iron make it particularly useful in treating aged patients.

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MANAGEMENT OF CHRONIC DEPENDENCY IN OUT-PATIENT CLINICS BY A COMPREHENSIVE MEDICAL-PSYCHIATRY SERVICE

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The establishment of the Comprehensive Medical-Psychiatry Service at Mt. Sinai Hospital, Chicago, illustrates rather dramatically how research findings can be applied to the development of a new program providing a special form of care for the sick. A common, and often a most distressing and frustrating problem to all concerned is the patient who feels distressed and ill, who attends the out-patient clinic regularly, reports his aches and pains faithfully, comes even more frequently than requested, and yet the doctors can find only a limited basis for the many complaints. These patients are referred from clinic to clinic in the hospital, receive work-up after work-up and many series of laboratory tests and x-ray examinations. It is an expensive and disappointing process. Sometimes something is found, though usually not serious enough to warrant the amount of "illness" actually experienced. Certainly as these patients get older, it becomes easier to find such a "something." A great deal of their time and energy is taken up with illness; a great deal of medical and pharmaceutical time and material is also involved. Nevertheless, the patients continue to feel sick, to complain and to distress both themselves, their families, and the clinic staff. To tell them they are not sick and need not come back is hardly possible. To refer them all to psychiatry as "mental cases" is neither practical nor helpful They are chronically ill, and dependent on the clinic for medical care. They want relief and help. What can we do for them?

1954–1956 PROGRAM

In July 1954 a research team headed by Dr. Harry H. Garner of the Chicago Medical School and the Mt. Sinai Hospital staff—including Miss Eleanor Scher, Director of the Samuel A. Goldsmith Dispensary and Mrs. Dorothy Morwitz, Director of Social Service Department and their staffs—undertook the study of a consecutive series of such patients who had been attending the out-patient clinics of Mt. Sinai Hospital for over two years and had averaged one or more visits a month during that time. Their findings were published in the January 1957 issue of the Journal of Mental Hygiene in an article entitled "A Study of Chronicity in Medical Clinics." Finances for this investigation came from the Mental Health Fund of the State of Illinois.

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One hundred and ten such patients were exhaustively reviewed. Medical status was assessed, and the life history was taken by a social worker. A clinical psychologist estimated the intellectual and personality resources and potentials through a standard series of tests. A psychiatrist appraised the mental state, the structure of the personality, and the quality of life adjustment generally. Each case was reviewed by the research staff in conference, and recommendations were submitted to the hospital personnel for treatment. In many cases the research team also followed the therapeutic procedures for demonstration purposes.

The ages of these patients ranged from 50 to 80, making the problem predominantly a geriatric one. About half of the group showed distinct signs of early senility, in withdrawal from social contacts, diminution of activity, some memory loss of the recent past, and an increased preoccupation with their bodies. For most of them, visits to the clinics seemed to provide practically their only social or recreational contact. About one fourth of them had fairly clear-cut emotional disturbances of long standing; these cases could be diagnosed as standard psychiatric disorders which had gone unnoticed and untreated. The rest represented simple immaturity and personality dependence of long standing, the end-product being an adaptation achieved through the "respectability" of illness, to a life of inadequacy, stress and deprivations.

Attempts were made to help those patients that the research team believed could be benefited by social, psychologic, and/or psychiatric treatment. The Social Service Department made a study of the community resources available to enlarge the social life space of these people. Very soon 19 of them were active in recreation, Golden Age groups, hobby centers, or synagogue activities, without the type of concern they had had previously manifested about their illness. Four of them actually became employable, and found regular work. Thirty-eight were so dependent on the hospital that they refused to join outside groups, but consented to attend group therapy sessions led by the psychologist and social workers. Twelve were registered for individual psychotherapy. The important finding was that something constructive could be done socio-psychologically for a little over half of this group of patients.

Comment. When the total program was reviewed in March 1956, it was found that: 1) more than one third of the patients had shown no change, or were attending clinics at an increased rate; 2) in the more responsive group, the ready availability of many clinics and the many attending physicians to whom they could go as sick people, seemed to be a constant temptation for back-sliding; and 3) such patients seemed to cluster in 2 or more of the following 5 clinics: Medicine, Gastrointestinal, Cardiac, Metabolism, and Arthritis.

1956–1958 PROGRAM

During the summer of 1956, on the basis of these 3 research findings and experiences of the 1954–56 period, the project entered a new phase in which the emphasis was on service and action, rather than on research. It was believed that the social structure of the clinic itself, in which the same patient may be seen by

different doctors in the same clinic from visit to visit, and is seen by different doctors in different clinics, tended to encourage both "shopping around" by the patient, and referrals to each other by busy clinic physicians. Accordingly, the Mental Health Fund of the State of Illinois agreed to continue support of the psychiatric aspects of the program, and permitted some of the authorized funds to be used in setting up for a one-year demonstration, a special Comprehensive Medical-Psychiatry Clinic to provide an integrated medical, psychiatric, psychologic and Social Service team which would give total care. The staffing plan provided for: 1) An internist who would furnish total medical care in place of the 5 clinics, using them when in his opinion a consultation was required. The patients remained active in such other clinics as they had been attending for the time being, pending the results of the demonstration. 2) A psychiatrist to collaborate in the diagnostic assessment of all cases, to treat selected cases, to consult on psychogenic factors with other members of the team, and to recommend the lines of psycho-social therapy. 3) A psychologist to evaluate intellectual, psychologic, and vocational potential, and to administer group and individual psychotherapy. 4) A social worker to make available the life history and the current socio-environmental data, to inform on the available community resources, to prepare patients for transfer to this clinic, and to work with the families of the patients. The Comprehensive Medical-Psychiatry clinic got under way in July, 1956 with the transfer of 151 cases by the 5 clinics. Through August 1957, 201 cases were referred, bringing the total number served to 352. Referral of new cases has proceeded at a monthly rate of about 25.

All these patients were seen by one physician, Dr. Milton Handelman, an internist. Thus the attention of the patient was focused in one doctor-patient relationship, instead of being diffused among many. The doctor was thus enabled to see the patient as a whole rather than as a fragmented individual, the fragment being the particular organ or organ system for which the specialized clinic is established. It was found that the patients followed recommendations more consistently. There was also a diminished use of other clinics, since many minor problems could be treated without referral. Another intent—withdrawing the medical sanction given the patient's "sick role" by reducing the frequency of clinic attendance to the patient's objective medical needs—was accomplished more satisfactorily when the patient was handled by one doctor. The doctor has a sense of security in management. He has at his fingertips the complete social and psychologic pictures, and can rely on his team mates to detect any stresses produced by these factors. Thus he can help the patient to make a new adjustment to the idea of not being so sick, with the help of social and psychologic services.

There was complete acceptance of the service by the patients. They were delighted to have all their illnesses correlated and treated by the same observer. They felt more and more secure as the doctor-patient relationship developed. Before new patients were taken on in the clinic, they were interviewed by the social worker, Mrs. Villarosa, and given an interpretation of the service and an opportunity to tell their story. For most, this was their first chance to relate

themselves in a dynamic way to one person in the hospital who was interested in them as a total human being. The social worker explained the purpose and goals of the clinic, and how talking with the psychiatrist and psychologist, as well as with her, might offer some help in improving their situation. The routine nature of what, under other circumstances, might have been a threatening or frightening referral, made for a maximum of cooperation. The emphasis was on helping the staff to understand the patients, rather than to discover whether they were mental cases.

Comment. The overall impression of the program has been a favorable one. The other clinics have had a resource to which they could refer this frustrating type of patient whose care requires so much time, attention, and ancillary services. Patients themselves initiated referrals, as word of this clinic spread among them, and a status value gradually accrued. The arrangement became likened by them to having a "private doctor," especially as more intimate interpersonal relations developed with the clinic personnel, and the dependence was transferred from the many to the fewer people with whom they had to deal. At a given point, they more readily accepted a reduction in medical attention, and a reduction in the doctor's sanction of their sickness by assurance that they were better able to do well outside, and that they could get a more immediate appointment if it was really needed. Many of these patients are now being seen at intervals of four to six months. Another advantage which accrued medically was the fact of continuous review of the patient through time by the same personnel. Work-ups became more adequate. Errors of omission were reduced. Closer observation assured earlier detection of malignancy. Such a program delays and reduces hospitalization, and institutionalization of various types. When disabling illness supervenes, integration with the Home Service facilitates re-entry to the clinic when the patient is able to make the visits. A more healthy emotional tone is established through the interest demonstrated in a total program involving several professional disciplines.

Social Service. The social service program was vital in the achievement of the patient's readiness to accept a reduction in his "sick role" and function as a healthier person than he wanted to be. Preparation for this clinic was stressed, so that the patient was prevented from developing a negative orientation to this new set of experiences. Emphasis was placed on their positive meaning, especially when the reduction in medical attention is initiated. The social worker was then called upon to talk with the patient and with any relatives who might not be so ready to accept this idea. Encouragement in turning interests and energies outward towards the environment became a basic case work procedure. In turn, the familial and community environment required motivation to accept this new social role of the patient. Vocational services, activity programs in the community, camps, Golden Age groups, sheltered workshops, and homemaking services had to be located and collaboratively supported in their efforts to enable these patients to move out of the clinic and their limited social world. Just as the patients needed preparation for turning to the outside, the outside needed preparation in meeting the patients in an optimistic, hopeful way. Medical social case work with the patients and their families served to alleviate stress in

interpersonal relationships, and to allay any anxiety or misunderstandings that clinic activity, home medical service, hospitalization and nursing care may have aroused in the course of the hospital's work.

This total clinic population would not be conventionally thought of as a good source of cases for medical social case work. In following up the initial interviews, however, the medical social worker found that she had given significant service during the year to 96 patients; in 18 of these, the service could be considered intensive, in 28 it was intermediate, and in 50 it was a short-term contact.

Psychologic and Psychiatric Services. The psychologist of the service, Mr. John McAllister, continued the testing of all new referrals, participated in staff planning sessions, and continued the group therapy program. This program dealt with groups of 10 to 20 patients who were considered ready to meet in this manner under the clinic's auspices but who did not yet have enough courage to venture out into the community. The Chief of Adult Psychiatry, Dr. A. Hilkevitch, arranged for examination and diagnostic evaluation of all these patients. He selected those who would benefit from psychotherapy, and indicated those whose neurologic and emotional status was such as to constitute a limited potential for the kind of social and psychologic readjustment aspired to by the personnel. Eighteen cases were treated psychiatrically during the year.

General appraisal. At the close of the first year of operation a number of questions had to be answered in order to decide on policy for the coming year. Although the Mental Health Fund would continue to support the Psychiatric Service, medical care beyond the one year of demonstration would have to be financed by Mt. Sinai Hospital. Who were these patients? What were their sex, age, ethnic background, and the nature of their illnesses? Did this clinic and the attitude of denial of illness lead to an increased protestation of illness and an increase in clinic attendance, as some critics believed? Would the reduction of visits to the Comprehensive Medicine department increase visits to the other clinics, or to the Emergency Room, as some believed?

RESULTS

It was possible to tabulate the results of a full year of experience with the first 30 cases referred during August and September 1956. Most of these patients had attended 2 or 3 of the 5 clinics, as well as many others. At the onset, an attempt was made to differentiate between those "on relief" and those who were financially self-supporting; this was discontinued when only 1 non-relief case was disclosed among the first 20. We may conclude therefore that the group was a completely indigent population, dependent on public relief. Notwithstanding the changing nature of the neighborhood and population, this group was predominantly Jewish; only 4 of the 30 were non-Jews; 2 were Negroes. The age range was from 33 to 82 years; in 19 patients the age range was from 67 to 80 years.

The distribution by age and sex is shown in Table 1. The small number of cases makes the comparison by sex of questionable significance, but it is of interest that in the age group 76 and over, there were more men than women, despite the well known outnumbering of men by women at this age.

At the outset, we also attempted to tabulate by married state; however, only

TABLE 1

Distribution of 30 Comprehensive Medical-Psychiatry Clinic Patients by Age and Sex

Age (yrs.)	Male	Female	Total
55 and under	2	1	3
56–60	0	3	3
61–65	0	3	3
66–70	2	5	7
71–75	1	5	6
76–80	4	2	6
over 80	1	1	2
Totals*	10	20	30
Average age	*71*	*68*	*69.5*
* Supplementary data (sample, 132 cases):			
Totals	27	105	132
Average age	*73.5*	*68.7*	*71.6*

1 of the first 20 patients had a living spouse, so this tabulation was discontinued. For all practical purposes, the group under study was composed of widows and widowers, usually living alone, and dependent on public assistance.

The presenting or significant illnesses were: arteriosclerosis in 28, osteoarthritis in 13, diabetes in 7, and obesity in 8.[1] All of the patients with whom we started remained in the clinic, except 1 who was transferred to a hospital closer to home and dropped from the study. Two became atypical; one of these was transferred to Home Medical Service (HMS) and the other was hospitalized for five days. Each house call by the physician on HMS was equated to a clinic visit, and each day of hospital care was also equated to a clinic visit.

Table 2 shows the drop in clinic visits from a total of 704 in the year before initiation of the new clinic program to 459 in the year afterward—a decline of 245 or 35 per cent. This did not mean a diminution of attention, inasmuch as these patients were being seen by Psychiatry, Psychology and Social Service. The total number of these supplementary contacts were not included in the present study, which sought to establish only the effect on visits to physical medicine.

Instead of visiting the 5 clinics 307 times, they made 192 visits to the Comprehensive Medical Clinic—a drop of 115 visits, or 37 per cent. These same patients who had attended other clinics 329 times, made 223 CMC visits—a drop of 106 visits, or 32 per cent. The decline in emergency visits to the house doctor was 24—from 68 to 44, or 35 per cent.[2]

Table 3 shows the total clinic visits before and after transfer.

[1] A later tabulation (sample of 132 out of 596 cases) showed the following distribution: arteriosclerosis 104, osteoarthritis 83, diabetes 39, obesity 34, and hypertension 23.

[2] A later tabulation involving a sample of 132 cases showed even greater reductions—47, 29 and 29 per cent, respectively.

TABLE 2

Frequency of Clinic Visits for the First 30 Patients Before Transfer, Compared with Frequency After Transfer to Comprehensive Medical-Psychiatry (CMP) Service

No. of Clinic Visits	No. of Cases in 5 Clinics Before Transfer	No. of Cases in CMP Clinic After Transfer	No. of Cases All Other Clinics		No. of Cases—Emergency House Doctor Visits	
			Before transfer	After transfer	Before transfer	After transfer
2–5	4	12	6	16	26	28
6–9	12	14	11	4	3	2
10–13	7	3	3	4	1	—
14–17	3	—	3	2	—	—
18–21	2	1	2	1	—	—
22–25	2	—	3	1	—	—
26–29	—	—	2	2	—	—
Totals*....	307 visits	192 visits	329 visits	223 visits	68 visits	44 visits
Averages (30).....	*10.2*	*6.4*	*11.*	*7.4*	*2.3*	*1.5*
* Supplementary data (sample, 132 cases):						
Totals..	154 visits	839 visits	1228 visits	964 visits	423 visits	301 visits
Averages (132).	*11.7*	*6.4*	*9.1*	*7.3*	*3.2*	*2.3*

TABLE 3

Total Clinic Visits by the First 30 Patients, Before and After Transfer to Comprehensive Medical Psychiatry Service

No. of Clinic Visits	Before Transfer	After Transfer
2–5	0	5
6–9	0	8
10–13	6	2
14–17	5	6
18–21	6	1
22–25	2	2
26–29	1	2
30–33	3	1
34–37	3	1
38–41	1	1
42–45	1	0
50–54	2	1
Total*.....	704	459
Average.....	23.5	15.3
* Supplementary data (sample, 132 cases):		
Total	3179	2104
Average	24	16

DISCUSSION

The favorable experience of the clinic, its acceptance by the other clinic services, and the concrete evidence of reduction in clinic visits without discernible untoward effects, led to the establishment of the clinic as a permanent feature of the Out-patient Department, financed by hospital funds. The final step of recognition and acceptance was the administrative decision to make the clinic genuinely comprehensive. Instead of being limited to the 5 clinics, beginning October 1, 1957, all medical care for these cases was centralized in the Comprehensive Clinic. It is anticipated that this will make for an increased rate of progress in the indicated direction.

The Psychiatry Department of the Chicago Medical School has continued a research and demonstration interest in the clinic. A basic problem is that of the criteria for the selection of cases, and prognosis. If a limited potential for the absorption of new cases into the clinic should develop, the patients most likely to react favorably would be given preference until the clinic's capacity was expanded. A comparative study of the most successful and the least successful cases produced the following 2 typical pictures:

1) The least responsive patients exhibit a life pattern of immature, unstable dependent relationship, and their acceptance of the sick role has been a method of adjustment and a source of gratification. This acceptance of the sick role has been sanctioned by family, friends and physicians, and has established a pattern of secondary gains from illness. These persons are markedly resistive to any reduction in their sick role, resistant to any social or psychologic approach, and focus most of their attention on medicaments.

2) The most successful group are those who, in reaction to widowhood, retirement, separation from grown children, financial insecurity, loss of other intimate associates through mobility or death, and increasing debility, have in later life made a heavier and heavier investment in the social role of the sick person. In this role they have achieved recognition, response, attention, and a respectable defense for their decline in status, as long as they continue to secure some medical sanction by clinic attendance. Such persons are more amenable to methods of treatment which provide a reduction in the social role of sickness, a partial withdrawal of the physician's sanction of illness, and increased social participation and satisfaction in activities more commonly associated with health.

Consideration is also being given to the potential teaching advantages of such a clinic in orienting medical students and residents to the social environmental factors promoting illness, and how social and psychologic intervention may be used to further recovery. Too often the aged, chronically ill patient is received with irritation and pessimism. The removal of such patients from conventional teaching clinics creates a more favorable setting for teaching in the area of the acute illnesses, and provides a new setting for teaching the student a positive approach to geriatrics.

The student physician is enabled to see the patient as an individual, a member of a family, and of a social group, rather than a system of separate organs. The correlation between illness and loss of a spouse, between illness and economic

dependence or deprivation, between illness and rejection or neglect from children, and between illness and poor housing, malnutrition, inadequate physical care, or withdrawal from social contacts and social activities—all these correlations contribute to understanding the geriatric patient and his treatment. Because such patients constitute a growing segment of the average doctor's practice, a constructive approach must start with the experience of the student physician.

This bird's-eye view of the origins, development, and final establishment of a Comprehensive Medical-Psychiatry Clinic at Mt. Sinai Hospital, Chicago, illustrates uniquely how a special combination of research, demonstration, and teaching interests can be marshalled in order to deal constructively with a special problem—the chronically ill, dependent, geriatric patient—so that his welfare, the community's interests, and an extension of the frontiers of knowledge and education may simultaneously be served. It is believed that a real opportunity exists to demonstrate in a specific way that such a Comprehensive Medical-Psychiatry Clinic can arrest or decelerate the progressive degenerative process which tends to be fatalistically accepted in this type of illness. It is believed that such a clinic in conjunction with currently established Home Medical Services can keep such patients longer in the community and postpone or avoid forms of institutionalization which are too readily available. Any means of avoiding institutional life would be of significant benefit both to the patient and to the community. Research is being continued in order to establish statistical evidence as to whether or not this type of clinic is the treatment of choice for the chronically ill, dependent, geriatric patient.

Abstracts of Current Literature

LA CORTISONE DANS LE TRAITEMENT PRÉVENTIF ET CURATIF DES ACCIDENTS DE LA RADIOTHÉRAPIE EN O.-R.-L. (CORTISONE IN THE PREVENTIVE AND CURATIVE TREATMENT OF COMPLICATIONS FOLLOWING RADIOTHERAPY IN OTORHINOLARYNGOLOGY).

Appaix, A.; Pech, A.; Aymard, J., and Simon, M. *Presse méd.* **65:** 989, 1957; through Ciba Literature Review **2:** 337, 1957.

Irradiation of carcinomas in the ear, nose, and throat region frequently leads to the formation of edema or to inflammatory complications with severe sequelae. At best, more or less violent pain develops. Almost complete dysphagia also can occur, or tracheotomy may become necessary. If complications commence early, they may compel interruption of treatment. If they arise later, they impair the patient's general condition. Radiotherapy causes a syndrome similar to that encountered in cases of adrenocortical insufficiency. It was, therefore, likely that corticosteroids would exert a beneficial influence upon these complications, producing local improvement by reason of their anti-inflammatory effect and systemic improvement because of their hormonal action. The good response obtained in the treatment of complications following radiotherapy prompted a trial of prednisone in 26 patients, for prophylactic purposes as well. By administering 20 mg. of prednisone daily, it was possible to avoid such complications. Only one-third of the patients complained of slight anorexia or asthenia. Upon completion of radiation therapy, the leukocyte count was above 6,000 in every case, and the erythrocyte count above 4 million. Cutaneous or mucosal reactions that occurred in 3 patients were mild and temporary.

CLINICAL EVALUATION OF CHLOROTHIAZIDE (DIURIL) AS A DIURETIC AGENT IN CONGESTIVE HEART FAILURE.

Becker, M. C.; Simon, F., and Bernstein, A. *J. Newark Beth Israel Hosp.* **9:** 18 (Jan.) 1958.

Chlorothiazide (Diuril) was administered for its diuretic effect for periods of four to twenty-eight weeks in 50 patients as follows: rheumatic heart disease, 11; arteriosclerotic heart disease, 21; hypertensive heart disease, 5; hypertensive arteriosclerotic heart disease, 8; idiopathic myocarditis, 1; Paget's heart disease, 1; arteriosclerotic-pulmonary heart disease, 3. Four patients had previously received no diuretic agents, 4 had received only an oral preparation, and 32 had received parenteral diuretics alone or in combination with an oral preparation. The dosage was individualized and varied from 0.5 Gm. every other day to 1 Gm. twice daily. Doses higher than 2 Gm daily proved no more effective. The diuretic response was interpreted as excellent in 29 patients, good in 17, fair in 1, and poor in 3. Thirty-five patients required no further diuretics; this group included the patients who had received only oral diuretics previously or none, and 27 who had previously received parenteral medication alone or in combination with oral preparations. During the use of chlorothiazide, 6 patients required mercurial diuretic agents parenterally once a month or less frequently. These were usually required because of dietary indiscretion or respiratory infection. The dosage of drugs parenterally in 6 severely ill patients could be reduced. Poor patient cooperation and the advanced stage of arteriosclerotic heart disease in the patients in whom chlorothiazide was ineffective may explain this failure. A smooth continuous diuresis was obtained with less fluctuation in weight and symptomatology. There was a marked diminution in acute episodes of congestive heart failure such as paroxysmal dyspnea and pulmonary edema. There were no cases of resistance to chlorothiazide. Transient dizziness, weakness, occasional nausea, parasthesias, and leg cramps were noted in 3 patients and could be eliminated by reduction in dosage. No electrolyte imbalances were noted in 10 patients in whom these studies were made. None of 4 deaths in the group

could be attributed to the medication. No hypotensive effect of chlorothiazide was demonstrated in normotensive or diseased persons. The drug may have some antianginal effect but this must be further investigated.

THE TREATMENT OF ARRHYTHMIAS AND SHOCK WITH MEPHENTERMINE SULFATE IN LARGE DOSES. A PRELIMINARY REPORT.

Bernstein, A.; Cohen, F.; Robins, B., and Simon, F. *J. Newark Beth Israel Hosp.* **9:** 3 (Jan.) 1958.

Mephentermine sulfate (Wyamine), or N-methylphenyl butylamine sulfate, possesses pressor, positive inotropic, and antiarrhythmic actions and can be injected intravenously or intramuscularly. This substance was evaluated using larger than recommended doses, in 10 cases of shock; 5 of these patients had proved myocardial infarctions and 5 had shock of noncardiac origin. The dose was 45 to 60 mg. intravenously immediately, followed by an infusion of 600 mg. in 500 ml. of 5 per cent dextrose in water. The drug produced an effective rise in blood pressure in 8 of the 10 patients and corrected the arrhythmias in 2 of them. Failure was noted in 1 patient with peritonitis and in 1 patient in Addisonian crisis. The blood pressure response with mephentermine sulfate occurred within ten to sixty minutes, without the need for the careful titration required with norepinephrine. The drug remained effective for varying lengths of time. In only 1 case of myocardial infarction did mephentermine sulfate fail when norepinephrine was effective, and the latter also failed in time. This was interpreted to mean that the infarct was of such size that the cardiac output was inadequate to maintain blood pressure, rather than that there was a failure of pressor activity. No slough, thrombophlebitis, or local reaction developed at the site of infiltration in any patient. It is concluded that mephentermine sulfate is valuable in the treatment of shock and worthy of further investigation.

THE USE OF VITARESPITAL IN THE TREATMENT OF ELDERLY PSYCHOTIC PATIENTS.

Blackman, L. H.; Glenn, A., and Olinger, L. *Internat. Rec. Med.* **171:** 46 (Jan.) 1958.

Vitarespital, a combination of reserpine, *d*-amphetamine, and therapeutic vitamins was used to treat 43 elderly psychotic patients, while 39 others received placebo medication and served as controls. The group comprised the following: senile psychosis, 41; psychosis with cerebral arteriosclerosis, 18; dementia praecox, 10; manic depressive psychosis, 4; involutional psychosis, 3; psychosis due to syphilis, 3; alcoholic psychosis, 2; post-traumatic psychosis, 1. The 39 men were between the ages of 47 and 84 years, with an average age of 66 years. The 43 women were between the ages of 55 and 95 years, with an average age of 75 years. The physical and mental status of all patients was evaluated prior to the adminisration of Vitarespital. This preparation and the placebo medication were administered three times daily for five weeks. Improvement occurred as follows in the percentages of patients indicated: nutrition, 92; sphincter control, 35; muscle strength, 41; sociability, 76; cooperation, 56; activity, 56; initiative, 50; and self-care, 56. Approximately 10 per cent of patients receiving Vitarespital needed no sedation, although it had previously been required. Approximately 8 per cent showed improvement in sensorium and 12 per cent were less depressed. No significant changes in blood pressure occurred.

COAGULATION DURING HYPOTHERMIA IN MAN.

Bunker, J. P., and Goldstein, R. *Proc. Soc. Exper. Biol. & Med.* **97:** 199 (Jan.) 1958.

Coagulation studies are reported in 10 patients (5 men and 5 women, aged 18 to 70 years) before and after slow cooling and during surgery at lowered body temperature. The diagnoses were cerebral vascular aneurysm, 4; meningioma, 3; cerebellar hemangioblastoma, 1; and thoracic aortic aneurysm, 2. Clotting times, platelets, thromboplastin generation, pro-

thrombin consumption, prothrombin time, and concentrations of prothrombin, accelerator globulin, proconvertin, and fibrinogen were measured before and after the slow induction of hypothermia and during surgery and transfusion. Hypothermia itself was not associated with significant disturbances in any of the specific clotting factors measured. During hypothermia, surgery, and transfusions, moderate disturbances in factors of the first and second stages of coagulation were observed. With the exception of a depression of prothrombin consumption, these resembled the disturbances seen during surgery and transfusions in patients at normal body temperature. The depression of prothrombin consumption was marked in 3 patients and moderate in 3 others. It could not be explained by the degree of thrombocytopenia or by the alteration in thromboplastin generation found in 2 patients. A qualitative change in platelets was not excluded, and plasma factors concerned with thromboplastin formation were not measured separately. Prolongation of clotting times for all coagulation tests except whole blood clotting times was consistently observed when performed at hypothermic temperatures rather than at 37.5°C. Studies of clotting were made postoperatively in 2 patients. Moderate depression of platelets and accelerator globulin present at the end of surgery in 1 patient persisted for two days but returned to normal or above after one week. Moderate increases in most clotting factors occurred in both patients after one week, and in 1 there was moderate thrombocytosis.

INTRACAVITARY OR INTERSTITIAL USE OF ISOTOPES IN CARCINOMA OF THE URINARY BLADDER.

Cuccia, C. A. *J. Urol.* **79:** 94 (Jan.) 1958.

The discovery of new radioactive isotopes has brought about over-enthusiasm and some misunderstanding about the value of such means of treatment. The isotopes in the 2 primary categories, beta and gamma ray emitters, have certain indications and limitations, but within the categories they are fundamentally the same. Consideration is given to the use of isotopes intracavitarily or interstitially. The choice between agents is mainly dependent upon technical considerations. The primary task is to select the cases that present the right indications for each of the procedures. I. Multiple small noninfiltrating lesions in stage 0 and stage A: Intracavitary isotopes (Na-24, Br-82, Au-198) in liquid form, which are mainly beta emitters, are used in this type of lesion. The objective is to deliver a high dosage of radiation to the superficial structures—the infiltration must not pass the submucosa in order to spare the peripheral parts of the viscus that are not affected. Br-82 is preferred over Na-24 because it contains more gamma rays. Radioactive gold in dust form applied directly to the bladder offers some advantages over the intracavitary method with the substance in liquid form in a bag because the papillary growth is surrounded by the isotope with better irradiation, but it is useful only for superficial lesions no thicker than 3 mm. II. Multiple lesions of the urinary bladder with infiltration of the muscle, stage B_1: Intracavitary gamma ray emitters are used for these lesions in order to give uniform irradiation to the whole bladder with a dose of increased depth. It is essential that the radiation source (radium, or cobalt-60) be placed in the exact center of the inflated bag. III. Single infiltrating lesion of the bladder, not larger than 5 cm. in diameter: This type of lesion is treated interstitially with any gamma ray emitter. This delivers a high amount of radiation 0.5 cm. from each side of the plane of insertion. Therefore, thicker tumors must be shaved off in order that the infiltrating base remains no thicker than 1 cm. The different forms of the isotopes available permit different technics of insertion. Thus, a flexible implant of tantalum wire is preferable to the implantation of rigid radium needles. It is easily inserted and can be withdrawn through the urethra when the treatment is completed. Gold grains which are regular in shape and easy to obtain may be substituted for radon seeds which have been widely used. Gold grain and cobalt in nylon threads are flexible sources and represent a technical improvement. IV. Deeply infiltrating lesions, stage B_2 or C: These lesions are not suitable for intracavitary or interstitial treatment. The likelihood of spread at the edges would mean that viable cells would probably be present outside the irradiated area.

PHYSIOLOGICAL ASPECTS OF AGING. I. EFFICIENCY OF ABSORPTION AND PHOSPHORYLATION OF RADIOTHIAMINE.

Draper, H. H. *Proc. Soc. Exper. Biol. & Med.* **97:** 121 (Jan.) 1958.

Experiments in rats on the absorption of an oral dose of C^{14}-labeled thiamine showed that approximately 95 per cent was absorbed by rats up to the age of 19 to 20 months, whereas only 75 per cent was absorbed by those which were 22 to 24 months old. Neither normal nor excess quantities of thiamine in the diet caused the absorption to differ from that in thiamine-deficient animals. A low proportion of absorbed radiothiamine was found in esterified and unesterified forms in the livers of the old rats as compared with that in rats 5 to 8 months old.

LA PRÉDNISONE À DOSE MASSIVE DANS LE LYMPHOGRANULOME, LE LYMPHOSARCOME ET LE RÉTICULOSARCOME (MASSIVE DOSAGE PREDNISONE IN LYMPHOGRANULOMA, LYMPHOSARCOMA, AND RETICULOSARCOMA).

Dubois-Ferrière, H. *Schweiz. med. Wchnschr.* **87:** 1228, 1957; through Ciba Literature Review **2:** 369, 1957.

Eight patients with lymphogranuloma, 2 with reticulum-cell sarcoma, and 1 with lymphosarcoma were treated with large doses of Ultracorten (prednisone). All of these patients, who previously had received radiation therapy or cytostatic agents, were in such poor general condition that radiologists had refused to give them further radiation therapy. Ultracorten was administered orally for three to seven days in doses of 600 to 1,000 mg. daily. One female patient received in addition 200 mg. of Ultracortenol (prednisolone) parenterally. In all cases, a complete clinical remission was obtained. Adenopathies, exudates, pulmonary infiltration, and swelling of the liver and spleen disappeared. The patients became afebrile and no longer suffered from pruritus. The remission, as a rule, lasted two to three months. In the event of a relapse, Ultracorten again proved effective. The period of well being brought about by Ultracorten affords an opportunity to administer cytostatic agents or radiation therapy. The mechanism of action of massive doses of Ultracorten is unknown and probably differs from that of the usual doses. It seems likely that the beneficial response is due, not to replacement or simulation of endogenous hormones, but to the antimetabolic effect exerted by Ultracorten.

IL QUADRO SIEROPROTEICO NELL'IPERTENSIONE (SERUM PROTEINS IN HYPERTENSION).

Franzini, D., and Mosna, S. *Progr. med.* **13:** 193, 1957; through Ciba Literature Review **2:** 359, 1957.

With the aid of various methods (paper electrophoresis, Boselli's euglobulin analysis, serum colloid reactions), the changes in serum proteins were studied in 33 hypertensive patients, of whom 22 had essential hypertension, 6 hypertension with atherosclerotic complications, and 5 chronic glomerulonephritis and hypertension. All the patients showed a moderately severe dysproteinemia, that is, increase in the level of total serum proteins, relative decrease in albumins and increase in globulins, particularly the alpha and gamma fractions, with inversion of the protein quotient. These changes in serum proteins are present at the beginning of hypertension, but become more marked after a few years. They are particularly clear-cut in patients with vascular lesions due to atherosclerosis or diabetes. In patients with contracted kidney of glomerulonephritic origin, on the other hand, the alterations are not pronounced. It is interesting that the progressive rise in blood pressure connected with aging of the body causes the same dysproteinemia as essential hypertension. From a practical point of view, it may be said that the serum protein findings supply valuable information about the course of hypertension and can also indicate both improvements and deteriorations.

ARTERIOGRAPHY OF THE UPPER EXTREMITY.

Gaffney, C. J.; Hershey, F. B., and Allen, W. E., Jr. *Surg., Gynec. & Obst.* **106:** 63 (Jan.) 1958.

The percutaneous injection of the subclavian artery, at the site where it crosses the first rib, with sodium diprotrizoate (Miokon) has been tested in 19 cases and found to be a safe and convenient method for the radiographic demonstration of the arteries of the upper extremities. The only contraindication to the use of this substance is hypersensitivity. Therefore, a test dose of 1 cc. is given intravenously prior to injection of the medium. The method is described. A dosage of 20 to 30 cc. of 30 per cent sodium diprotrizoate is injected into the subclavian artery within ten seconds. The first film is exposed at the end of the injection. Serial films may be taken and are particularly helpful in the case of arteriovenous fistulas and occlusive disease in which the circulation time is altered. By this method, the larger arteries of the arm, the forearm, and the palmar arch may be seen. It has proved useful in determining the patency of arterial anastomoses and in the evaluation and differential diagnosis of occlusive and vasospastic diseases. No morbidity, significant vasospasm, or complications were encountered in this series of patients. The medium has the advantage that it causes little pain, swelling, or inflammation upon accidental extravasation. It has not been necessary to expose the subclavian or brachial artery nor to occlude the artery to slow the flow of the injected medium. Visualization of the arteries of the hand is possible if a larger volume of solution and more concentrated medium are used. As with all arteriograms, the success of this method depends upon the selection of the proper position of the extremity, the correct dose of the medium, the rate of injection, the timing of the films, and the use of the smallest volume of the most dilute medium that will permit adequate visualization.

BEITRAG ZUR MEDIKAMENTÖSEN AMBULANTEN BEHANDLUNG PSYCHISCH KRANKER (CONTRIBUTION TO THE AMBULATORY MEDICAL TREATMENT OF PSYCHIC DISORDERS).

Gschlacht, V. *Praxis* **46:** 1037, 1957; through Ciba Literature Review **2:** 357, 1957.

One hundred and nine ambulatory patients aged 20 to 79 years, who were suffering from various psychic disorders, were given Ondasil (each tablet contains 125 mg. of Doriden with 0.1 mg. of Serpasil) or Ondasil forte (double strength tablets) in addition to psychotherapy. The average daily dosage was 3 to 4 tablets, and the maximum single dose did not exceed 2 tablets of Ondasil forte. The duration of treatment varied from three weeks to twelve months. Ondasil exerted a prompt tranquilizing and relaxing effect, thus creating better conditions for psychotherapy. The response was particularly good among patients with autonomic nervous dystonia. Ondasil has a damping, that is, normalizing, effect on overshooting impulses, particularly those of the autonomic nervous system. In various forms of neuroses, Ondasil facilitates or supports psychotherapy. It also alleviates the tormenting abstinence symptoms in addicts undergoing withdrawal cures and thus reduces the risk of a relapse at the beginning of the cure. Two patients with depression attempted to commit suicide at the commencement of treatment by taking 30 tablets of Ondasil forte each. After sleeping for twenty-four hours, they awoke without complications. Slight side-effects occurred in 8 patients but did not necessitate discontinuation of therapy. No signs of addiction were observed.

EFFECTS OF TEMPORARY ISCHEMIA ON RENAL FUNCTION UNDER NORMAL AND HYPOTHERMIC TEMPERATURES WITH AORTIC RENAL GRAFT REPLACEMENT.

Hardin, C. A., and Valk, W. L. *Surg., Gynec. & Obst.* **106:** 82 (Jan.) 1958.

Experiments were performed on dogs to study the effect of temporary ischemia on kidney function under normal and hypothermic conditions. Following this, operations were per-

formed on 2 patients in whom the renal arteries were involved by abdominal aneurysm and tumor, respectively, so that a period of renal ischemia of approximately one-half hour was required in order to complete resection and graft replacement of the surgical defect. Hypothermia afforded some protection to the kidneys in these patients. Postoperatively, studies of renal function showed impairment. Further studies showed a gradual return of function but not to normal. Although both operations were initially successful, the patients died after two and six months, respectively—the first from hemorrhage caused by the rupture of a distal iliac vessel, and the second from repeated upper gastro-intestinal tract hemorrhage associated with hiatus hernia.

SYSTEMIC VERSUS LOCAL FACTORS IN CORONARY ARTERY OCCLUSION.

Holman, R. L.; Enos, W. F., Jr.; Beyer, J. C., and Manion, W. C. *United States Armed Forces M. J.* **9:** 12 (Jan.) 1958.

An investigation was carried out to determine whether a metabolic tide of systemic origin or a purely local circulatory disturbance such as vasoconstriction precipitates disease referable to arteriosclerosis, since it has been shown that beyond age 3 all persons have some degree of atheroma in the aorta and that by the end of the second decade three-fourths of all persons have some atheroma in the coronary arteries. Histologic sections of aorta and coronary arteries were examined from the following groups from whom both were available: 1) unselected cases of recent myocardial infarction (males, aged 21 to 81 years), 18; 2) coronary artery occlusion in males below 30 years of age, 41; 3) selected cases of acute occlusion of the coronary arteries (1 woman, 4 men; aged 26 to 44 years), 5; 4) asymptomatic persons with inanition, from the Dachau prison camp, who died of various causes other than coronary occlusion or infarction (males, aged 17 to 65 years); 5) asymptomatic control cases from two sources: (a) American males aged 18 to 29 years, 20; (b) Japanese persons 14 to 45 years of age (3 females, 7 males), 10. Most of the sections in these studies were "routine" sections stained with hematoxylin and eosin. The sections of aorta were those selected without a definite purpose in mind. In the study of the last two groups, that is, the planned studies, stains for fat were used and other special stains in selected cases. Data interpreted as being consistent with the concept of a metabolic tide consisted of the finding of recent foam-cell collections in lesions of both the aorta and the coronary arteries. These were taken to represent the active phase of atherosclerosis. Recent collections of foam cells were found in both the aorta and coronary artery plaques in about 45 per cent of those persons who died from a coronary occlusion and in about 10 per cent of those whose death was due to other causes. This lends support to, but does not substantiate, the concept of a metabolic tide. Other findings of interest in support of this concept were that the lesions in the sections of the aortas and coronary arteries of young adult males were usually in the same phase. Thus, if the lesions in the aorta were composed primarily of altered ground substance, so were those in the coronary arteries. If the former contained clusters of foam cells or basal grumous material, so did the latter. If evidence for 2 accretions was found in one site, it was also found in the other. The scant evidence in this study favors episodic accretion.

ADMISSIONS OF GERIATRIC CASES TO A MENTAL HOSPITAL.

Horbaczewski, J. *Canad. M. A. J.* **78:** 22 (Jan.) 1958.

Many elderly persons who require medical or surgical treatment, or prolonged nursing care, are being sent to mental hospitals on the grounds that they may be delirious or mildly confused, irascible, or alienated from the environment by improper management. Two-thirds of admissions to mental hospitals consist of patients who are crippled, incurable, and requiring terminal care for neoplastic disease or for advanced cachexia, and who show only mild or no mental aberration but may be poor or have no interested relative. Unnecessary crowding of mental hospitals with patients such as these can be avoided if certain common conditions in elderly people which may cause temporary confusion or delirium are remembered on evaluation of their medical status, and treated outside the mental institution.

These conditions are: (a) uremia due to prostatism, nephrosclerosis, pyelonephritis, chronic glomerulonephritis; (b) cerebrovascular accidents; (c) congestive heart failure; (d) diabetic acidosis; (e) septicemia; (f) chronic constipation; (g) chronic starvation; and (h) abuse of sedatives. Incurables and cripples without acute psychotic symptoms should be accommodated in appropriate nursing homes. The present practice of sending these patients to mental hospitals should be considered a disservice to the community as it conceals the necessity of a better solution of geriatric problems, invalidates the statistics for mental patients, and consumes the limited resources and energy of the mental hospitals which should be devoted entirely to the treatment of mentally ill patients. Homes for the aged should tolerate patients with slight irascibility and mild disorientation. (Excerpt of author's summary.)

PREDICTIVE VALUE OF LIPOPROTEIN AND CHOLESTEROL DETERMINATIONS IN DIABETIC PATIENTS WHO DEVELOPED CARDIOVASCULAR COMPLICATIONS.

Lowy, A. D., Jr., and Barach, J. H. *Circulation* **17:** 14 (Jan.) 1958.

This paper represents a part of the U. S. Public Health Service research project that was designed to determine if the lipoprotein molecule and cholesterol determinations have any predictive value for ensuing atherosclerotic complications. There were 690 diabetic patients examined from 1951 to 1953, and for 606 of these follow-up data in the subsequent two to five years could be obtained. In the group followed there were 61 new atherosclerotic events consisting of myocardial infarction, angina pectoris, arteriosclerosis obliterans, and cerebral vascular accidents. The mean lipid values in the patients with complications were elevated and sometimes significantly elevated as compared to those most evident in the females age 40 to 59 and to a lesser extent in the males age 60 and over. When the analysis was performed by quartiles, more than 50 per cent of the complications occurred in patients whose lipid determinations were above the median. These differences were significant for the males age 60 years and over and for females aged 40 to 59 years. In the age group 14 to 39 years, there were only 2 males and 2 females in whom complications developed, and no definite conclusions can be drawn even though the results appear favorable. The lipid measures as a predictor of vascular complications in diabetic patients are not applicable to any one individual. For a large group, the patients with higher values, however, tend to have a greater number of complications. The increased chance of complications varies with age, sex, and the particular lipid measure. The cholesterol value as a predictor is as good as, if not better than, the pattern of the lipoprotein molecules; and the complexity and expensiveness of the S_f molecule determination make its use impractical for clinical purposes. (From authors' summary.)

PSYCHODYNAMICS OF THE PERSONALITY CHANGES IN THE AGED.

Prados, M. *Canad. Psychiat. Assoc. J.* **2:** 177 (Oct.) 1957.

Statistics on first admissions of elderly persons to mental hospitals show a growth beyond the normal rise of the older age group in the community. This situation presents many practical problems not only for the psychiatrist in the mental hospital, but also for the social psychiatrist and for the private practitioner. Research has indicated that psychosis in the elderly may not be explained exclusively upon the basis of lesions in the brain, but that emotional and environmental factors also play an important role in many behavior difficulties. A dynamic approach to the problem has produced encouraging results. An aged person can respond favorably to psychotherapy provided one follows the principles of a dynamic approach. The climacteric, like puberty, is a period during which the ego must use all its resources in order to make an adequate adaptation to a new situation. During puberty the adolescent notes the intensity of his instinctual tendencies, while during his climacteric, the person has to learn to adapt to simultaneous internal and external modifications which he experiences as profound injuries to his narcissistic needs. He must adapt himself during this period, although it is precisely the time when his capacities for adaptation are diminished. His success will depend primarily, but not exclusively, upon the forces of ego that he

will have succeeded in building during his life. Environmental and cultural factors, as well as individual circumstances such as physical health, play an important role in the success or failure of this adaptation. The psychiatrist who wishes to make a psychotherapeutic approach must take into account all of these factors. Even if they appear to undergo less difficulty at the climacteric, men are less prepared than women to accept the arrival of senility. When a woman has accomplished her task with respect to propagation of the race, she feels herself more capable of using her capacities in new social tasks, being freed of the anxiety that accompanies the reproductive function. Man, on the other hand, complains that society contains more and more pressing exigencies, and his ego is less and less strong. Furthermore, he believes himself much more strongly than the female to be in competition with the young, and he always feels obliged to compete with them, even if it kills him. After a last resurgence of sexuality in both male and female, regression commences; the behavior of the aged will be determined further by pregenital impulsions and modalities. However, this situation can be considerably ameliorated because aged persons in general show a greater capacity to accept unpleasant facts, are less inclined to consider as menacing the demands of reality. Furthermore, they present a tendency towards introspection. These various characteristics considerably facilitate the therapeutic approach, so that the aged person can obtain better comprehension of his difficulties much more readily than is generally believed. (From author's summary.)

THE EARLY DETECTION OF GLAUCOMA. RESULTS OF 2000 ROUTINE TONOMETRIES.
Reed, H., and Bendor-Samuel, J. E. L. *Canad. M. A. J.* **78:** 6 (Jan. 1) 1958.

Early cases of glaucoma in which vision is not yet damaged and there is no optic atrophy are likely to be overlooked. If detected in the early stage, visual deterioration can be prevented or delayed. The performance of tonometry routinely in persons over the age of 40 years appears to be the best way of discovering these early cases. It allows the early rise in intraocular pressure to be detected. When increased intraocular pressure is found in this way, the diagnosis of glaucoma can be confirmed by several methods: 1) gonioscopy enables one to distinguish between narrow-angle glaucoma which tends to give rise to acute attacks of increase in intraocular pressure with pain, blurring of vision and the appearance of haloes around lights, and wide-angle glaucoma which progresses slowly; 2) inasmuch as intraocular pressure varies throughout the day, repeated tonometric measurements may be necessary to determine the presence of glaucoma; 3) in the water-drinking test, a rise of more than 6 mm. of mercury within the first hour after the patient drinks a quart of water is diagnostic of wide-angle glaucoma; 4) a similar rise after the instillation of a mydriatic is positive evidence of narrow-angle glaucoma; 5) a decreased rate of flow (a coefficient less than 0.15) of aqueous humor from the eye when a tonometer is resting upon it indicates the presence of glaucoma. Among 2000 routine ophthalmic examinations in persons over the age of 40 years, 28 cases of glaucoma were diagnosed by history and clinical examination alone, but 71 patients who clinically were normal had raised intraocular tension by routine tonometry. Thirty of these patients were shown to have glaucoma. Signs of the disease will probably develop in another 7 patients. Thus, glaucoma was present in 3 per cent of persons over the age of 40 years and was diagnosed by tonometry in 2 per cent. It was considered that one of the latter would have been missed for each case recognized by clinical examination had it not been for routine tonometry. It is recommended that general practitioners learn this test and use it as a part of the physical examination of patients over the age of 40 years and that medical schools include it in the instruction of undergraduates.

A NEW APPROACH TO THE SURGICAL MANAGEMENT OF PEPTIC ULCER BY GASTRECTOPLASTY.
Shoemaker, W. C., and Martin, W. L. *Surg., Gynec. & Obst.* **106:** 105 (Jan.) 1958.

Numerous operative procedures have been proposed for attaching the gastric remnant to the jejunum or duodenum following partial removal of the stomach. Some have concerned

ways to mobilize the duodenum and gastric remnant for gastroduodenostomy. A technic is described which is believed to be the first attempt to deal directly with the gastric pouch remaining after high partial gastrectomy. The pouch is lengthened, in order that gastroduodenostomy may be achieved, by making an incision 6 to 8 cm. long on the anterior wall of the pouch at the junction of the upper and middle thirds, and a similar incision in the posterior wall at the juncture of the middle and lower thirds. At the upper third of the pouch, the anterior and posterior walls are closed with a continuous inverting mattress suture. The suture is continued, joining the flaps created by the incisions in "Z" fashion, so that the gastric pouch assumes a cylindrical appearance. This operation has been performed on 9 patients, 5 with duodenal ulcer, 3 with gastric ulcer, and 1 with carcinoma of the stomach. No deaths occurred and no unusual consequences. The patients have been followed for two months to one year. Achlorhydria was the rule postoperatively, except in 1 patient with 15 clinical units of free acid after histamine. Roentgenograms of the gastrointestinal tract showed satisfactory function. There have been no nutritional defects, nor failure to gain weight. Three case reports illustrate the results with this plastic procedure.

CRANIOPHARYNGIOMAS IN THE AGED.

Tiberin, L.; Goldberg, G. M., and Schwartz, A. *Neurology* **8:** 51 (Jan.) 1958.

Craniopharyngioma probably occurs in elderly persons more frequently than the few reports on it indicate. It may not be diagnosed because of variations in its mode of onset and symptomatology. Two cases in elderly women are presented. The symptoms varied between them and from those of patients reported in the literature. Therefore, there may be no characteristic symptomatology in craniopharyngioma in the aged. In each of these patients, mental deterioration was the outstanding manifestation and obscured less striking features. Its presence should be cause for further investigation. Findings common to those of intrasellar space-occupying lesions in the first patient led to an erroneous diagnosis of pituitary adenoma. The associated frontal lobe symptomatology (grasping, hyperactive reflexes, and pyramidal signs) may have been caused by interference with the blood supply, as demonstrated by angiographic examination. The bradycardia, relative hypothermia, and hypotension were probably due to direct involvement of the hypothalamus. Loss of consciousness marked the onset in the second patient. Electroencephalograms helped to localize the process. Pneumoencephalography in this patient suggested a diagnosis of third-ventricle tumor, which was incorrect. Postoperative shock in the first patient, and the fatal outcome postoperatively in both patients, make it clear that patients with hypothalamic lesions and pituitary failure are not likely candidates for craniotomy.

PSYCHOLOGICAL REACTIONS OF THE AGED IN SURGERY. THE REACTIONS OF RENEWAL AND DEPLETION.

Titchener, J.; Zwerling, I.; Gottschalk, L., and Levine, M. *A. M. A. Arch. Neurol. & Psychiat.* **79:** 63 (Jan.) 1958.

A psychiatric, psychological, and social study of 45 randomly selected and representative surgical patients 65 years of age and over is reported. Deterioration of mental capacity progressed in 11 patients during their hospital surgical treatment. The following etiologic factors were significant: (a) Patients aged 70 and over were more liable to progression of mental deterioration. (b) The acute brain syndrome or delirium preceded chronic deterioration in 7 patients. (c) Antecedent anxiety, depression, and severe emotional disturbances were associated with later deterioration in 9 patients. (d) Patients who had lost an accepting and comfortable home environment were more liable to deterioration. Depression of a disabling kind appeared in 22 of the 45 patients. This affect was forced by a complex combination of psychodynamic factors, including perception of lack of capacity to resist everyday stress, hostility and guilt, perception of defect in body image, loss of self-esteem, impairment of ability to remain active, and threat to self-preservation. Projection and

paranoid ideation were significant psychopathologic phenomena in 9 patients. Principally, this reaction occurred in response to the real or imagined indifference of those persons significant to the elderly patients. Two over-all responses of the aged to surgery are described—the reactions of "renewal" and "depletion." Renewal is intended to characterize a self-concept of repair, hope, and freedom to continue activity and a capacity to invest affect outside the individual. Depletion is intended to characterize an awareness or half-awareness of a sense of personal deterioration, with lessened capacity to meet stress and a need to draw resources inward, to withdraw, and to mobilize for self-preservation. It is theorized that the psychodynamic effect of the reaction of depletion has pathophysiologic consequences. (Authors' summary and conclusions)

EXFOLIATIVE CYTOLOGY OF THE SENILE FEMALE URETHRA.

Youngblood, V. H.; Tomlin, E. M.; Williams, J. O., and Kimmelstiel, P. *J. Urol.* **79:** 110 (Jan.) 1958.

That the urethra lends itself to cytologic study has been given little attention. Cytologic study was used to demonstrate the reason for benefit obtained by the local application of estrogen in cases of senile urethritis. Urethral smears from 25 postmenopausal women with urethral irritation were studied cytologically before and after treatment with Furacin urethral suppositories containing 0.1 mg. of diethylstilbestrol, applied to the urethra twice daily for one week or once daily for two weeks. The ages of the patients were between 45 and 102 years, with an average of 61 years. In 20 of the women, the initial smears showed predominantly basal cells. A response to estrogen was exhibited by the presence of intermediate and superficial cells after treatment. In 5 women, the smears initially showed superficial epithelium and remained unchanged by treatment, indicating that these were not cases of senile urethritis and that senile and nonspecific urethritis cannot be differentiated clinically. These results are in accord with the findings of Zuckerman (1940) that the urethra, as a derivative of the urogenital sinus, retains the capacity to react to female hormone. They show that signs of irritation produced by an atrophic urethra can be relieved by estrogen.

NEWS AND NOTICES

RECORD OF 1958 LEGISLATIVE ACHIEVEMENTS FOR THE AGED IN THE STATE OF NEW YORK

Promote employment of older workers: 1) Enacted an historic anti-discrimination law for the 40-plus job seeker; it outlaws refusal to hire any job seeker 45–65 because of age. 2) Authorized expansion in staff of special job counsellors for the 40-plus, first set up by GOP legislation, and now resulting in placement of about 4,000 hard-to-please older job seekers, and 250,000 other older job seekers. 3) Banned discrimination against the 40-plus job seeker in public authorities. 4) Banned discrimination against the 40-plus by school boards.

Prevent poverty in old age: 1) Raised *minimum* pensions of retired teachers to $1,800 a year, providing some 6,000 retired school teachers with a pension increase. 2) Provided $25,000 to the State Social Welfare Department to develop experiments designed to prevent poverty in old age as, for example, retraining projects, and counselling. 3) Extended to July 1, 1959, ability of retired state employees to earn additional money in public employment by working part-time or seasonally.

Improve health insurance for the aged: 1) Prohibited insurance companies from cancelling or refusing to renew hospital and medical insurance policies which have been in force for 2 years, except for fraud or other good reason. 2) Required conversion privileges without evidence of insurability to person who had been a member for 3 months and applies within 1 month. 3) Required that any age limitations in a policy be stated in large type on face of policy. 4) Required conversion privileges for persons leaving a family group.

Combat loneliness in old age: 1) Raised formula for state-aid to recreation centers for aged from 10¢ per person to 25¢; increased appropriation to $200,000 a year; and expanded the aid program to include towns as well as cities.

Encourage housing for the elderly: 1) Passed a public housing bond referendum bill to provide $75,000,000 for low-rent housing, of which, in accordance with previously sponsored legislation requiring the set-aside of specially designed units for the aged, some $7,500,000 will be allocated for housing the aged. 2) Passed a $100,000,000 middle-income housing referendum bill under which non-profit groups such as religious, welfare agencies will be able to obtain low cost loans for providing low-rent housing for the aging. 3) Encouraged families to house grandparents by exempting pensions up to $75 a month from income limitations in public housing projects.

Aid the chronically ill: 1) Exempted sheltered workshops in municipal hospitals from paying unemployment insurance and workmen's compensation taxes. 2) Appropriated $100,000 to finance a study of how to extend Blue Cross coverage. 3) Voted large-scale appropriations for cancer research at Roswell Park Memorial Institute in Buffalo, for rehabilitation of adults at New York State Rehabilitation Hospital, and the Chronic Disease Research Institute which is being developed into a center for heart disease research.